# Irritable bowel syndrome in the general population: epidemiology, comorbidity, and societal costs

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Helsinki 2010

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ACADEMIC DISSERTATION

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*To Anu, Petri, and Taru*

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# List of original publications

This thesis is based on the following publications, which are referred to in the text by their Roman numerals I-IV:

I Hillilä MT, Färkkilä MA. Prevalence of irritable bowel syndrome according to different diagnostic criteria in a non-selected adult population. Alimentary Pharmacology & Therapeutics 2004; 20: 339-345.

II Hillilä MT, Siivola MT, Färkkilä MA. Comorbidity and use of health-care services among IBS sufferers. Scandinavian Journal of Gastroenterology 2007;(42)7:799-806.

III Hillilä MT, Hämäläinen J, Heikkinen ME, Färkkilä MA. Gastrointestinal complaints among subjects with depressive symptoms in the general population. Alimentary Pharmacology & Therapeutics 2008; 28: 648–654.

IV Hillilä MT, Färkkilä NJ, Färkkilä MA. Societal costs for irritable bowel syndrome – a population based study. Scandinavian Journal of Gastroenterology, in press.

# Abbreviations

| | |
|---|---|
| BDI-SF | Beck Depression Inventory Short Form |
| CI | Confidence interval |
| CNS | Central nervous system |
| ENS | Enteric nervous system |
| FD | Functional dyspepsia |
| fMRI | Functional magnetic resonance imaging |
| GERD | Gastro-oesophageal reflux disease |
| GI | Gastrointestinal |
| IBS | Irritable bowel syndrome |
| IBS-C | IBS with constipation |
| IBS-D | IBS with diarrhoea |
| IBS-M | Mixed IBS |
| IgE | Immunoglobulin E |
| κ | Cohen's kappa value |
| M | Million |
| NNT | Number needed to treat |
| PAN | Primary afferent neuron |
| PEG | Polyethylene glycol |
| PET | Proton emission tomography |
| QoL | Quality of life |
| R-BDI-SF | Raitasalo-Beck Depression Inventory Short Form |
| SERT | Serotonin transporter |
| SSRI | Serotonin reuptake inhibitors |
| TCA | Tricyclic antidepressant |
| 5-HT | 5-hydroxytryptamine |

# Abstract

**Background:** Irritable bowel syndrome (IBS) is a functional gastrointestinal (GI) disorder characterised by abdominal pain and abnormal bowel function. The diagnosis of IBS is based on symptom description as no organic, biochemical or structural abnormalities are present. In epidemiologic studies, the prevalence of IBS ranges between 3 and 25%, usually with an over-representation of the female gender. The wide variation in prevalence estimates is partly due to various IBS definitions and diagnostic criteria. The most frequently used symptom based criteria include Manning, Rome I, and Rome II criteria. Manning criteria generally give a higher prevalence estimate than Rome II criteria.

IBS is associated with a high rate of psychological and somatic comorbid conditions, such as depression, anxiety, dyspepsia, headache, lower back pain, and fibromyalgia. Moreover, IBS is associated with a high rate of health care consumption for both GI and non-GI reasons. IBS sufferers miss work for illness almost three times as often as controls. Therefore, IBS incurs significant direct and indirect health care costs for society.

The aim of this study was to assess the prevalence of IBS among subjects of working age according to various diagnostic criteria. In addition, we studied the rates of somatic and psychiatric comorbidity and health care consumption for GI and non-GI reasons, as well as predictors of health care seeking. Finally, we evaluated the societal costs of IBS.

**Methods:** The study was a two-phase postal survey. In phase I, a questionnaire covering GI symptoms according to Manning 2 (at least two of the six Manning symptoms), Manning 3 (at least three Manning symptoms), Rome I, and Rome II criteria, was mailed to 5 000 randomly selected non-institutionalised Finnish residents aged 18 to 64. The questionnaire also included a Finnish modification of the Beck Depression Inventory Short Form (BDI-SF) and items covering the severity of GI symptoms, rates of headaches, back pain, and dyspeptic symptoms. In addition, health care consumption for GI and non-GI reasons and work absenteeism for GI reasons was inquired. In phase II, a questionnaire covering rates of GI health care visits in primary and secondary care, use of GI medication, and the duration of GI symptoms, was sent to subjects fulfilling IBS criteria according to Manning 2 or Rome II criteria in the phase I questionnaire.

**Results:** The response rate was 73% and 86% for questionnaires I and II. After adjusting for age and gender, the prevalence of IBS was 15.9% (95% CI 14.7-17.1%), 9.6% (95% CI 8.6-10.6%), 5.6% (95% CI 4.8-6.4%), and 5.1% (95% CI 4.4-5.8%) according to Manning 2, Manning 3, Rome I, and Rome II criteria. Of those meeting Rome II criteria, 97% also met Manning 2 criteria.

The prevalence of depressive symptoms in the general population was 16.7% (95% CI 15.4-17.9%). Of subjects with depressive symptoms, 11.6% met Rome II IBS criteria compared to 3.7% of those with no depressiveness ($p < 0.0001$). In addition, subjects with depressive symptoms reported more physician visits and sick leave days for GI symptoms than those without.

Presence of dyspeptic symptoms, lactose intolerance, headache, back pain, depressive symptoms, anxiety, and insomnia was more common among subjects meeting any IBS

criterion than by controls not meeting the criterion. In addition, presence of asthma or an allergic condition was more common among those fulfilling Manning 2, Manning 3, or Rome II criteria than among controls. Presence of severe or very severe abdominal pain and disturbance of daily activities by abdominal pain were more often reported by subjects meeting either of the Rome criteria than those meeting either of the Manning criteria.

During the previous year, a larger share of subjects meeting any IBS criteria had made GI and non-GI physician visits than controls. In addition, subjects fulfilling either of the Rome criteria more often reported GI physician visits than those fulfilling either of the Manning criteria. Intensity of GI symptoms and presence of dyspeptic symptoms were the strongest predictors of GI consultations, but also headaches, insomnia, and presence of a chronic illness were independent predictors. For non-GI visits, presence of chronic illness, back pain, and depressive symptoms were the strongest predictors. In addition, presence of dyspeptic symptoms and a history of abdominal pain in childhood also predicted non-GI visits.

Annual GI related individual costs were higher in the Rome II group (497€, 95% CI 382-621€) than in the Manning 2 group (295€, 95% CI 246-347€). The nationwide annual GI related expenses were higher by Manning 2 criteria than Rome II criteria (154M€, 95% CI 128-181M€ vs. 82M€, 95% CI 63-103M€). Direct expenses of GI symptoms and non-GI physician visits ranged between 98M€ for Rome II and 230M€ for Manning criteria.

**Conclusions:** The prevalence of IBS shows substantial variation depending on the criteria applied. Rome II criteria are more restrictive than Manning 2 criteria, and they identify an IBS population with more severe GI symptoms, more frequent health care use, and higher individual health care costs. In the general population, subjects with IBS demonstrate high rates of psychiatric and somatic comorbidity regardless of health care seeking status. Perceived symptom severity rather than psychiatric comorbidity predicts health care seeking for GI symptoms. Depressive symptoms are prevalent in the general population and they are associated with an elevated rate of GI symptoms, physician visits, and work absenteeism for GI symptoms.

IBS imposes a significant impact on national health care expenditures. The direct GI and non-GI costs of IBS are equivalent to up to 5% of outpatient health care and medicine costs in Finland. A more integral approach to IBS by physicians, accounting also for comorbid conditions, may produce a more favourable course in IBS patients and reduce health care expenditures.

# 1. INTRODUCTION

Irritable bowel syndrome (IBS) is a chronic functional gastrointestinal (GI) disorder characterised by abdominal pain or discomfort and altered bowel habits. The aetiology of IBS is multifactorial with altered visceral sensitivity, altered gastrointestinal motility, and psychosocial factors influencing symptom generation.

The prevalence of IBS varies worldwide, affecting 3 to 25% of the population. Up to 90% of subjects with IBS demonstrate comorbid somatic or psychiatric symptoms. They make more health care visits than the control population without IBS. Work absenteeism due to IBS symptoms is as frequent as that of common cold. Direct and indirect costs of IBS incur considerable societal economic burden.

The definition and diagnostic criteria of IBS has changed over time. In 1978 Manning *et al.* presented the first symptom based criteria for IBS, widely applied later in epidemiological research. In 1989, the Rome criteria were introduced and later modified as Rome I, Rome II, and Rome III criteria.

The wide variation in the prevalence of IBS may reflect true differences between various populations and countries. Differences in IBS definitions and study methodologies, however, hamper reliable comparison between previous studies.

The main aim of this thesis was to assess the prevalence of IBS according to varying diagnostic criteria in a randomly selected population sample and to compare sociodemographic, symptom characteristics, and health care use between subjects meeting varying IBS criteria and a control population. The thesis also aimed to compare rates of comorbid psychiatric and somatic conditions between those meeting IBS criteria and a control population, and evaluate their influence on the use of health care facilities among IBS sufferers. In addition, societal costs of IBS were to be evaluated.

# 2. REVIEW OF THE LITERATURE

## Definition, natural history, and prognosis of irritable bowel syndrome (IBS)

In medical literature, a description of IBS-type symptoms can be found as early as 1820[1]. The symptoms included "occasional pain in the intestines and derangement of their powers of digestion, with flatulence, and a sense of suffocation". Since that, these symptoms have been given names such as "spasmodic stricture of the colon"[2], "mucous colitis"[3], "neurogenic mucous colitis"[4], "colonic spasm"[5], and "irritable colon syndrome"[6]. Nowadays, IBS is defined as "a functional bowel disorder in which abdominal pain or discomfort is associated with defecation or a change in bowel habit, and with features of disordered defecation"[7]. The term "functional" refers to absence of any organic disease, or structural or biochemical abnormality causing the symptoms. Abdominal pain or discomfort relieved by defecation indicates a possible colonic source, and appearance of pain associated with a change in bowel habits is indicative of a change in intestinal transit time, which may be a result of a change in intestinal motor or secretory function[8].

Symptoms of IBS follow a chronic relapsing course. After one to ten years of follow-up, 50 to 70% of subjects still fulfil IBS criteria[9-11]. The mean duration of GI symptoms among current IBS sufferers ranges between 5 and 13 years. A long history of GI symptoms and ongoing life stress are predictors of persisting symptoms[8].

IBS is a benign disorder with no reported increased mortality in itself[12]. IBS is, however, associated with an increased level of abdominal surgery[13,14], which may, together with unnecessary medical procedures, produce a source of elevated mortality rate not detected in studies so far[15]. Despite a benign nature, IBS reduces the quality of life (QoL) similarly to organic diseases, such as gastro-oesophageal reflux disease (GERD), asthma, or migraine[16].

## Pathogenesis

The pathogenesis of IBS is not fully understood. Abnormal motor function, visceral hypersensitivity, abnormal central nervous processing of visceral stimuli, gastrointestinal infections, subtle inflammation, psychosocial factors, abnormal gas handling, alterations in gut microflora, and genetic factors are possible agents involved in the pathogenesis of symptoms in IBS[17].

The enteric nervous system (ENS) is a neural network coating the GI tract. Together with the sympathetic and parasympathetic system it forms the autonomic nervous system. The ENS integrates the contraction of smooth muscles, intestinal transport of water and electrolytes, intestinal secretion, and intramural blood flow. It contains sensory and motor neurons, interneurons and several neurotransmitters, such as serotonin (5-hydroxytryptamine; 5-HT), acetylcholine, opioids, noradrenaline, somatostatin,

cholecystokinin, substance P, and vasoactive intestinal polypeptide. It functions semi-autonomously, receiving input from the motor outflow of the sympathetic and parasympathetic systems and sending sensory information to the central nervous system (CNS)[18,19]. According to a biopsychological conceptualisation, the brain-gut interaction between psychosocial and physiological factors influence GI symptom generation and outcome in terms of perceived symptom severity and medical care seeking[20] (Figure 1).

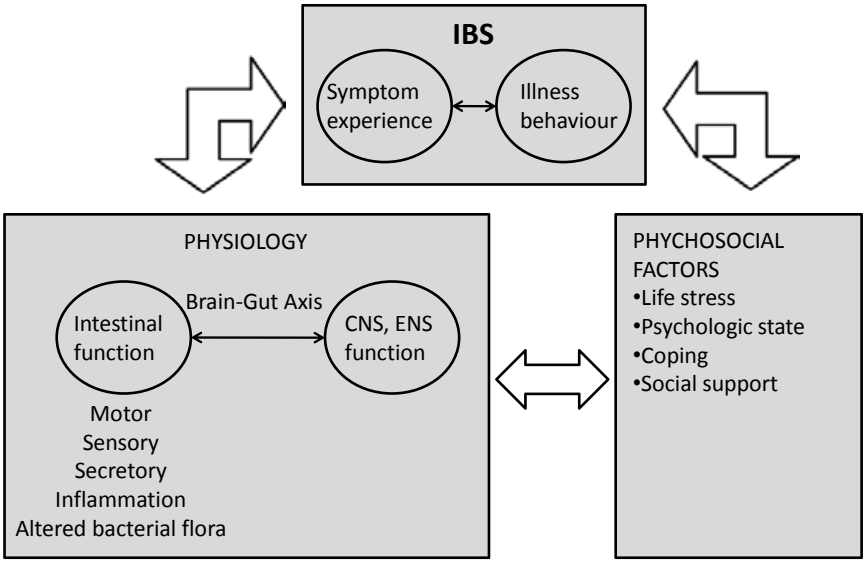


**Figure 1**. IBS conceptual model. IBS, irritable bowel syndrome; CNS, central nervous system; ENS, enteric nervous system.

Proximal colonic transit is accelerated in IBS with diarrhoea (IBS-D)[21]. In idiopathic constipation, both slowing of the whole colon and left colon transit is reported[22]. Also, altered small bowel transit with a correlation of GI symptoms[23] and abnormal response to stimuli, such as food and fatty acids, have been described[24].

IBS patients have a lower visceral pain threshold for both mechanical distension[25-27] and electrical stimuli[28,29] than controls, suggesting that primary afferent neurones (PAN) of the enteric nervous system are hypersensitive to non-noxius stimuli[30]. Some studies indicate that they also have cutaneous hyperalgesia[28,31,32].

Functional magnetic resonance imaging (fMRI) and proton emission tomography (PET) studies show aberrant brain activation during noxius rectal distention and in the anticipation of rectal pain among IBS patients[33-35], suggestive of abnormal central processing of the visceral stimuli. In an experimental fMRI study, amitriptyline reduced pain related cortical activation in IBS patients under stressful conditions[36]. In a PET study,

cognitive therapy reduced limbic activity, GI symptoms, and anxiety[37], suggesting that cortical processing influences IBS symptoms. In addition, rectal stimulation at distension pressures below conscious perception show abnormal CNS activation in IBS patients, suggesting hypersensitivity of the neural circuitry irrespective of stimulus-related cognition[38].

Depression, anxiety, psychological distress, and stressful life events are more common among subjects with unexplained medical symptoms and increased use of healthcare services[39]. Regardless of healthcare seeking status, an association between IBS and psychiatric distress has been established[40-42]. In addition, over-representation of physical or sexual abuse has been reported in IBS patients[43-45]. Psychiatric disorders, especially anxiety, may precede the occurrence of GI symptoms and thus have a pathogenetic role in the development of IBS, with a link to affective sprectrum disorders[46,47].

Infectious gastroenteritis precedes the onset of IBS in 6 to 17% of IBS patients[48]. The relative risk of developing IBS after infection increases 10 to 12 times compared to uninfected controls[49,50]. An increased number of mucosal lymphocytes, EC cells, higher levels of proinflammatory cytokines, and increased gut permeability are associated with post infective IBS[51-54]. In addition, regardless of a history of gastroenteritis, neuronal degeneration in the jejunal myenteric plexus has been detected[55], as well as activation of the mucosal immune system, especially in IBS-D[56,57]. Inflammatory changes in IBS and functional dyspepsia have even been reported in duodenal mucosa[58]. A recent study found elevated levels, similar to those in active ulcerative colitis, of faecal human β-defensin-2 in IBS-D and mixed IBS (IBS-M) patients compared to healthy controls, supporting an activation of the mucosal innate defence system[59]. IBS patients also have an increased frequency of activated T and B cells in their blood, consistent with a low grade inflammation[60,61]. One study reported a correlation between the severity of abdominal pain and activated mast cells in close proximity to mucosal nerve endings, suggestive of a peripheral mechanism of pain[62]. Moreover, IBS-D patients have displayed enhanced proinflammatory cytokine release associated with GI symptoms and anxiety[63].

Abdominal bloating, reported by up to 96% of IBS patients, is often the most bothersome symptom[64]. IBS patients have shown impaired gas transit, without signs of excess intra-abdominal gas[8]. Bloating alone is associated with visceral hypersensitivity, while patients with bloating and an increase in girth have normal sensory thresholds suggesting different pathogenetic mechanisms of the symptoms[65]. Bloating alone is reported more in IBS-D, while bloating with an increment in abdominal girth in IBS with constipation (IBS-C)[8].

Microbial genome analysis has revealed differences in the intestinal microbiota between IBS patients and healthy controls as well as between IBS subgroups, suggesting that intestinal bacteria also play a role in IBS development[30,66].

Genetic factors may influence development of IBS. Subjects who have a family member with GI symptoms are at a more than twofold risk of IBS-type symptoms, but having a spouse with these symptoms does not increase the risk[67]. Genetics appear to have a role in functional bowel disorders, since a concordance of 33% between monozygotic twins and 13% between dizygotic twins has been reported, referring to a 57% share for genetics and 43% for environmental factors in a model by Morris-Yates *et al.* [68]. Another

study concluded that social learning has an equal, or greater, influence than genetics on IBS development[69]. A genetic component has also been reported for extra-intestinal symptoms associated with IBS[70]. In addition, genetic polymorphism of serotonin transporter (SERT) may have a role in GI symptom pathogenesis[71,72].

## Diagnostic criteria

Diagnostic tests are performed to rule out organic diseases that may produce similar symptoms to IBS. Negative exclusion diagnosis by means of endoscopic, radiographic, and laboratory investigations is, however, costly and inconvenient for the patient. In order to turn IBS diagnosis into a positive symptom based diagnosis, Manning *et al.* introduced the first symptom-based diagnostic criteria for IBS in 1978 (Table 1). The more of the six symptoms present, the more accurately patients with IBS were discriminated from those with organic disease. Three of the six symptoms were pain related. In their study, 31 of the 32 outpatients with IBS had abdominal pain, but no information of the duration or frequency was given[73]. Two of the six symptoms were present in 94% of patients with IBS and 45% in patients with organic disease; the sensitivity was 94% and specificity 55%. Three or more criteria had a sensitivity of 84% and specificity of 76%[73]. In epidemiological studies, the required number of Manning symptoms to fulfil IBS criteria has usually been two or three[74-77]. For population studies, a cut off of two Manning symptoms have been suggested, because of a lower prevalence of organic diseases in the general population than among outpatients[78].

In 1989, a multinational committee of clinical-investigators published first Rome criteria for IBS diagnosis[79], originally presented at the Thirteenth International Congress of Gastroenterology held in Rome in 1988. IBS was defined as "a functional gastrointestinal disorder attributed to the intestines and associated with symptoms of: (a) abdominal pain, and/or (b) disturbed defecation, and/or (c) bloatedness or distension"[79]. Later, presence of abdominal pain was suggested as a requirement for the diagnosis, but the decision to do so was left to the investigator[80]. Terms such as spastic colon or irritable colon were no longer recommended. These criteria were revised later and published as the Rome I criteria[81] (Table 1). The main change from the 1989 criteria was the requirement of abdominal pain for IBS diagnosis. Rome I criteria consisted of abdominal pain related symptoms and non-pain related symptoms, later named the IBS supporting symptoms (Table 1).

The Rome I criteria were again revised, and the Rome II criteria published in 1999 by a Working Team[82]. The Rome II criteria were a committee consensus based on research results and expert opinion. The development process included reviewing and commenting by international experts. In the Rome II criteria, the second part, *i.e.* non-pain related symptoms of the Rome I criteria was deleted, due to poor clustering of these symptoms in factor analyses[83,84], their lower prevalence among males[85], and their partial inclusion in the first, pain-related part of Rome I criteria. In addition, "discomfort" was added to "pain", and symptom duration was extended from three months to 12 months, with abdominal pain or discomfort present for at least 12 weeks (not necessarily consecutive weeks)

(Table 1). Rome I and Rome II criteria have been developed for both clinical practise and research purposes, such as epidemiological surveys, pathophysiology research, and therapeutic trials.

In 2006, the Rome II criteria were again revised employing a consensus approach, leading up to publication of the Rome III criteria by the Rome Working Team[86] (Table 1). The main change concerned the time perspective: the diagnostic criteria must be fulfilled for the last three months instead of 12 months. In addition, symptoms had to have begun at least 6 months before clinical presentation addressing the chronic nature of symptoms.

Despite of wide use of the Rome criteria in research, their accuracy has received little study. For Rome I criteria, the sensitivity for detecting IBS was 85% and specificity 71% in a study of 602 patients[87]. In a retrospective study, Rome I criteria had a sensitivity of 65% and specificity of 100%, and positive predictive value of 100% in the absence of alarm signs[88].

## IBS subtypes

IBS can be divided into three subtypes according to predominant bowel habit. In IBS with constipation (IBS-C), stools are usually hard or lumpy, and bowel movement frequency is less than three per week. Straining during a bowel movement is common. In IBS with diarrhoea (IBS-D), stools are usually loose, mushy, or watery and bowel movements take place more than three times a day. In addition, urgency (having to rush to bathroom) is a common phenomenon. Mixed IBS (IBS-M) applies to subjects expressing both constipation and diarrhoea variably, for at least 25% of the bowel movements.[7] After a period of constipation, frequency of bowel movements typically increases leading to a period of diarrhoea. Usually these periods fluctuate rapidly within hours or a up to week[89,90]. Unsubtyped IBS refers to those not meeting the definition for IBS-C, IBS-D, or IBS-M, while Alternating IBS is recommended to define those whose IBS subtype changes to another over a longer, more than one year, period of time[89].

Each IBS subtype (IBS-D, IBS-C, IBS-M) forms about one third of the patients fulfilling the Rome II IBS criteria[89]. The proportion of the mixed subtype has varied between 23%[91] and 63%[92] in population based studies, however, and also IBS-D has been reported to be the commonest subtype[93]. During a three month follow-up, approximately half of IBS patients shift from IBS-C or IBS-D to IBS-M, but shifting from IBS-D to IBS-C, or vice versa, is less common[94].

The Rome II subtyping of IBS is based on non-pain related IBS supporting symptoms, while Rome III subtyping is based solely on stool consistency according to the Bristol Stool Form, which has shown good correlation with whole-gut transit time[95-98]. The validity of IBS subtypes is uncertain. In a comparison study, IBS subtypes defined by Rome II and Rome III criteria showed poor agreement[99].

**Table 1**. Manning, Rome I, Rome II and Rome III criteria for IBS.

**Manning criteria for IBS (Usually 2 or 3 symptoms required for criteria fulfilment)**

Looser stools at onset of pain
More frequent bowel movements at onset of pain
Pain eased after bowel movement
Visible (abdominal) distension
Passage of mucus
Feeling of incomplete evacuation

**Rome I criteria for IBS**

At least 3 months continuous or recurrent symptoms of:

1. Abdominal pain or discomfort which is:
   Relieved with defecation; and/or
   Associated with a change in frequency of stool; and/or
   Associated with a change in consistency of stool
   And
2. Two or more of the following, on at least a quarter of occasions or days:
   Altered stool frequency,
   Altered stool form (lumpy/hard or loose/watery),
   Altered stool passage (straining or urgency, feeling of incomplete evacuation)
   Passage of mucus,
   Bloating or feeling of abdominal distension.

**Rome II criteria for IBS**

At least 12 weeks or more, which need not be consecutive, in the preceding 12 months of abdominal discomfort or pain that has two out of three features:

1. Relieved with defecation; and/or
2. Onset associated with a change in frequency of stool; and/or
3. Onset associated with a change in form (appearance) of stool.

**Rome III criteria for IBS***

Recurrent abdominal pain or discomfort at least three days per month in the last three months associated with two or more of the following:

1. Improvement with defecation
2. Onset associated with a change in frequency of stool
3. Onset associated with a change in form (appearance) of stool

*Criterion fulfilled for the last three months with symptom onset at least six months prior to diagnosis

# Epidemiology

## Prevalence

The incidence of IBS shows a substantial variation ranging between 2 to 70 per 1 000 patient years[100-104]. In Western countries, the prevalence of IBS ranges between 3 and 25% of the population[92,103,105]. In non-Western countries, both lower prevalence estimates[106-108], and similar rates to Western countries have been reported[109].

Table 2 shows IBS prevalence in several population studies according to varying diagnostic criteria and gender. In general, the Rome II criteria give a lower prevalence estimate than the Manning criteria. Some studies have included only two of the six Manning symptoms, while others have required three symptoms. The more symptoms required, the lower the prevalence estimate of IBS, which partly explains the variation in prevalence estimates.

## Sociodemographic factors

In most studies, female gender is over-represented amongst IBS populations by a ratio of 1.5 to 2.0[77,100,105,110-114]. Some studies applying the Rome II criteria, however, report a female to male ratio closer to one[115-118]. IBS-C is more common among females than males, while IBS-D is more common among males[119-122]. Females more often report bloating and extraintestinal comorbidity[123].

Pain related symptoms (pain eased after bowel movement, pain related to change in bowel habits) are equally common in both sexes[84]. Symptoms not related to pain (diarrhoea, constipation, bloating, extraintestinal manifestations), however, are more common among female patients[85,123]. Inclusion of non-pain related symptoms may partly account for female over-representation in IBS by Manning criteria. According to some reports, Manning criteria are less reliable in males[124,125].

The prevalence of IBS is highest between 20 to 40 years old[126], and usually decreases with age[105,127].

Some studies report a decrease in IBS prevalence with increasing income[93,128], suggesting that IBS is more prevalent amongst the lower social class. On the other hand, affluent childhood has also been associated with adult IBS[129].

**Table 2.** Prevalence of IBS by varying diagnostic criteria

| Study | Population | Country | Method | Response rate (%) | n | IBS criteria | IBS prevalence All | Male | Female |
|---|---|---|---|---|---|---|---|---|---|
| Talley *et al.* 1991[78] | Olmsted County; random sample | USA | Postal survey | 82 | 835 | ≥ 3M | 12.8 | 12.1 | 13.6 |
| Heaton *et al.* 1992[77] | Physicians' registry sample | UK | Postal survey | 72 | 1 896 | ≥ 3M | 9.5 | 5.0 | 13.0 |
| Jones *et al.* 1992[110] | Physicians' registry sample | UK | Postal survey | | 1 620 | ≥ 2 M | 21.6 | 18.7 | 24.3 |
| Drossman *et al.*1993[105] | Random sample of households | USA | Postal survey | 66 | 5 430 | Rome 1989 | 9.4 | 7.7 | 14.5 |
| Österberg *et al.* 2000[42] | Random suburban sample | Sweden | Postal survey | 58 | 2 707 | Rome I | 10.6 | 7.4 | 13.3 |
| Boyce *et al.* 2000[75] | Random sample of electoral roll | Australia | Postal survey | 72 | 2 910 | ≥ 2 M | 13.6 | 9.8 | 17.2 |
| | | | | | | Rome I | 4.4 | 2.2 | 6.4 |
| | | | | | | Rome II | 6.9 | 4.6 | 9.2 |
| Talley *et al.* 2001[130] | Birth cohort of young adults | New Zealand | Questionnaire | 86 | 890 | ≥ 2 M | 12.7 | 10.8 | 14.6 |
| | | | | | | Rome II | 4.3 | 3.3 | 5.3 |
| Mearin *et al.* 2001[76] | Random population sample | Spain | Personal interview | 76 | 1 932 | ≥ 3 M | 10.3 | 5.6 | 14.8 |
| | | | | | | Rome I | 12.1 | 7.2 | 16.8 |
| | | | | | | Rome II | 3.3 | 1.9 | 4.6 |
| Bommelaer *et al.* 2002[131] | Random population sample | France | Postal survey | NR | 11 131 | Rome I | 4.0 | 2.5 | 5.3 |
| Saito *et al.* 2003[115] | Olmsted County; random sample | USA | Postal survey | 72 | 643 | Rome I | 6.8 | 5.6 | 8.0 |
| | | | | | | Rome II | 4.7 | 4.9 | 4.5 |
| Hungin *et al.* 2003[92] | Random population sample | 8 European countries | Telephone interview | NR | 41 984 | Manning | 6.5 | NR | NR |
| | | | | | | Rome I | 4.2 | NR | NR |
| | | | | | | Rome II | 2.9 | NR | NR |
| Dapoigny *et al.* 2004[132] | Random population sample | France | 2 phase postal survey | 76 and 83 | 15 120 | Rome II | 4.7 | 3.7 | 5.7 |
| Wilson *et al.* 2004[133] | Physicians' registry sample | UK | 2 phase postal survey | 62 and 78 | 4 807 | Rome II | 10.5* | 6.6* | 14.0* |
| Andrews *et al.* 2005[93] | Household sample | USA | Internet survey | 82 | 25 986 | Rome II | 6.6 | 4.7 | 8.2 |

≥ 2 M, At least two Manning symptoms

≥ 3 M, At least three Manning symptoms

*Including those with a previous IBS diagnosis by physician

NR, Not reported

## Comorbidity in IBS

About half of the IBS patients in primary care have at least one comorbid somatic symptom, and up to 94% of them have a comorbid psychiatric disorder[134]. The most frequently reported symptoms include fibromyalgia, headache, back pain, chronic pelvic pain, temporomandibular joint pain, pollacisuria, dyspareunia, heart palpitation, depression, anxiety, chronic fatigue syndrome, and somatoformic disorders. Most studies assessing comorbidity in IBS have been carried out in clinical settings, *i.e.* among health care users. In a population based study, IBS non-consulters have also demonstrated higher rates of psychiatric and somatic comorbidities than population controls[135].

Similarities occur in the demographic distributions and psychological profiles among IBS and many comorbid conditions, suggesting a possible common underlying pathophysiologic mechanism or a common underlying disorder with different manifestations, but the evidence of such factors is still missing[134].

### Psychiatric comorbidity

Depression and anxiety are common societal conditions. In a pan-European study, a 6-month prevalence rate for depressive disorders was 17%[136]. In the US, the life-time prevalence of major depression was 17% in the general population, and 25% had suffered an anxiety disorder[137]. In a Finnish population based interview study, the 12-month prevalence of a major depressive episode was 9.3%[138].

A comorbidity of depression, anxiety, and medical illness is also common. In the WHO Collaborative Study, primary health care patients with anxiety disorders were nine times more likely to develop depression than those with no other illness. Compared to patients with two or more chronic medical conditions, those with anxiety were six times more likely to develop depression. In addition, 39% of patients with depression also had an anxiety disorder, and 44% of those with an anxiety disorder also had depression.[139]

Patients with depression often present with overlapping somatic symptoms typically including medically unexplained pain[39]. Almost 30% of patients with depression also meet the criteria of IBS[140,141].

Patients with depression, or anxiety, use more healthcare services than those without. Amongst high utilizers of primary healthcare, 24% suffer from major depression, 33% have a lifetime history of depression, and 40% generalised anxiety disorder. In total, 83% of the high utilizers have psychiatric condition, including panic disorder, at some time in their lives.[142] Amongst patients with somatic medical conditions, the presence of a psychiatric condition, such as depression or bipolar disease, doubles the individual healthcare expenditures[143].

Mental distress and psychiatric symptoms are over-represented in IBS[42]. Common psychiatric diagnoses among IBS sufferers include generalised anxiety disorder, panic

disorder, post-traumatic stress disorder, and somatoform disorders including hypochondriasis and somatisation disorder[144-146].

Depression and anxiety are more prevalent amongst subjects with IBS than population controls or patients with somatic gastrointestinal conditions, such as inflammatory bowel disease[147]. Depression in IBS patients appears to be more common with females than males[148]. In primary care, patients with at least one GI symptom have a four to five fold prevalence of severe depression or anxiety compared to patients with no GI symptoms[149].

Psychiatric comorbidity may partly account for the higher level of healthcare use reported in IBS. Anxiety is particularly associated with healthcare seeking behaviour[108]. On the other hand, a strong association between IBS and psychiatric disorders have been found independently of healthcare seeking status[150].

## Somatic comorbidity

### *Gastrointestinal comorbidity*

Almost half of the IBS patients also manifest other GI disorders, such as functional dyspepsia (FD), GERD, functional constipation, and anal incontinence[151]. The separation of IBS, FD, and reflux has been criticised because of the poor clustering of these disorders in factor analyses and a strong tendency of subjects in epidemiological studies to flux between IBS, FD, reflux, and unspecified GI symptoms. Approximately 50% of subjects with GI symptoms such as IBS, functional dyspepsia, or reflux, change their symptom profile during a one year follow-up[9]. A possible common underlying mechanism or unspecific responses to patophysiological and psychological disturbances have been proposed to explain the variety of functional GI symptoms[9].

Up to 87% of the subjects with IBS also have FD[9,152]. Among IBS patients in a tertiary referral centre, IBS-C shows a higher rate of comorbidity with FD than other subtypes[153]. Co-occurrence of IBS and FD in primary care has been reported to increase referrals to secondary care[154].

GERD is a common symptom occurring in about 20% of subjects in the general population. IBS shows a substantial co-occurrence with GERD, as approximately 40% of IBS healthcare seekers also have symptoms of GERD[155].

Anal incontinence following first vaginal delivery has more frequently been reported (64%) in women with IBS compared to 10% without[156], possibly related to rectal hypersensitivity and hypocompliance, especially in IBS-D[157].

IBS has also been associated with a higher rate of abdominal surgery, especially subjects with psychiatric comorbidity. For example, cholecystectomy rates for IBS patients are three times as high as those for matched controls[13].

*Extraintestinal comorbidity*

Several nonpsychiatric extraintestinal symptoms are more prevalent in subjects with IBS than amongst non-IBS controls. In a US study, costs due to extraintestinal comorbidity covered more than 65% of costs incurred by IBS[158]. The most studied comorbidities are fibromyalgia, chronic fatigue syndrome, and chronic pelvic pain, all of which occur in 33 to 50% of IBS patients[151]. Population prevalence of fibromyalgia is 2%[159], chronic fatigue syndrome is 0.4%[160], and chronic pelvic pain occurs in 14% of females[151].

Chronic headache, migraine, temporomandibular joint disorder, and back pain are also significantly more common amongst IBS patients than healthy controls[151]. Besides chronic pelvic pain, other urogenital symptoms, such as dysuria, interstitial cystitis, dysmenorrhea, premenstrual syndrome, and disturbances in sexual function have also been reported more frequently than expected. Other symptoms include urinary stones, cardiac palpitations, and bronchial asthma or hyper-reactivity[161].

Many common underlying physiological mechanisms, such as smooth muscle disorder, immune dysfunction, inflammatory condition, neuromuscular disease accompanied by visceral hypersensitivity, female hormonal alterations, behavioural response to pain, alterations in serotonergic system, and psychological factors are possible links between IBS and extraintestinal comorbities. A theory of a global disease with symptoms covering multiple organs has not been proven to be the case. Multivariate analyses show comorbidities of IBS to be diseases of their own rather than a manifestation of a single disorder. IBS-sufferers with somatic comorbidities, however, possibly represent an IBS subgroup with psychological factors playing a common aetiological role.[151]

## Treatment options

The objective of treatment in IBS is to alleviate symptoms and increase QoL. A good patient-physician relationship is important for satisfactory treatment. The strength of the physician-patient relationship is inversely proportionate to the number of physician visits; a positive interaction between the physician and the patient has been associated with a reduced use of healthcare services[12,162]. Providing a diagnosis for the patient with an explanation of the benign nature of the symptoms will reduce fear of a malignant disease, help him or her to cope with the symptoms, and may even reduce the need for pharmacological treatment[163-165]. Factors worsening or triggering the symptoms, such as psychosocial stress or diet should be reviewed. In primary care, patients often attribute their symptoms to stress, but in secondary care are more likely to have psychiatric comorbidity, and consider stress unimportant for symptoms[166,167]. Patients seem to expect more benefit from advice for diet, lifestyle, and exercise than from drugs[168,169].

A total of 60 to 70% of subjects with IBS associate their GI symptoms with food sensitivity[170,171]. Dietary triggers reported to exacerbate IBS symptoms include caffeine, lactose, alcohol, fatty food, wheat, corn, citrus, food rich in carbohydrates, and hot spices[171-173]. Especially caffeine and lactose may exacerbate symptoms among subjects

with IBS-D. A poor correlation, however, exists between reported lactose intolerance and a true lactose malabsorption[174,175]. In addition, lactose restriction among subjects with IBS, reporting symptom exacerbation after lactose ingestion, does not necessarily improve GI symptoms[176,177]. Excess ingestion of fructose has also been associated with exacerbation of symptoms and occasionally a restriction diet may prove helpful[178,179]. No allergic IgE mediated reaction has been found to explain symptom exacerbation after meals[170,180]. Positive findings in some studies exploring the efficacy of food elimination diets may partly be due to a placebo effect, and due to lack of evidence, such diets are not routinely advised[181].

Increasing dietary fibre is generally recommended, though proof of efficacy of symptom alleviation is limited. Fibre products accelerate stool transit, and they are effective for treating constipation in IBS, but not pain or diarrhoea[182,183]. Moreover, insoluble fibre, such as wheat bran can even worsen symptoms such as abdominal bloating and flatulence[165,184-186]. For global symptom relief in IBS, soluble ispaghula husk seems to increase the rate of adequate relief and alleviate symptom severity, but insoluble fibre is no more effective than placebo[186-188].

Probiotics are live microorganisms capable of exerting health benefits on the host. Possible mechanisms of action include modulation of the host immune system, stimulation of defensive systems, and competitive decrease in the number of pathogens. Health benefits depend probably on the bacterial strain[189]. Bifidobacteria and probiotic combinations improve IBS symptoms, particularly flatulence and bloating, while lactobacilli alone does not seem efficient[181,190]. Optimal dosage and combination of probiotics are unknown at the time.

## Pharmacological treatment

The drugs available for IBS at the moment have limited evidence of efficacy. Less than one quarter of IBS patients demonstrate complete relief of IBS symptoms[92]. In addition, side effects of pharmacological therapies may have a considerable negative life impact[191]. The placebo effect is particularly strong, up to 70% in IBS drug studies[192]. Drug treatment is targeted to the dominant symptom or symptoms, usually diarrhoea, constipation, abdominal pain, or bloating.

Loperamide, a synthetic opioid, not transversing the blood-brain barrier, is effective in the treatment of diarrhoea by reducing stool frequency and improving stool consistency, but it is no more effective than placebo in reducing pain, bloating, and global symptoms of IBS[193-196].

In addition to dietary fibre supplementation and commercial fibre preparations for constipation, osmotic laxatives, such as lactulose, or polyethylene glycol (PEG) are commonly used, although little studied in IBS. Amongst subjects with functional constipation, a low dose PEG may be more effective and produce less flatulence than lactulose[197]. Amongst adolescents with IBS-C, treatment with a PEG laxative had a favourable effect on stool frequency, but not on pain intensity[198].

Smooth muscle relaxants and anticholinergic antispasmodics improve abdominal pain, but evidence of improving global IBS symptoms is not sufficient[181,199,200]. Generally these are taken on as-needed basis. Side-effects include dry mouth, dizziness, blurred vision, and constipation. Also, peppermint oil may be superior to placebo in alleviating IBS symptoms, possibly by relaxing smooth muscle[201,202].

Tricyclic antidepressants (TCA) and selective serotonin reuptake inhibitors (SSRI) alleviate neuropathic pain[203,204]. In IBS, TCAs have been used for abdominal pain. They have both anticholiniergic and non-selective serotonin reuptake actions. The neuromodulatory and analgesic features, thought to act by inhibiting visceral hypersensitivity, usually appear at lower doses than those used in the treatment of depression[36,205,206]. Anticholinergic side effects are similar to those with antispasmodics. Daily administration may bring out side effects even with low doses, however, the number needed to harm is 22[203]. According to a recent meta-analysis, the number needed to treat (NNT) is 4 (95% CI 3 to 8)[207]. A gradual introduction of TCA and a treatment duration of 6 to 12 months before dose tapering, has been suggested[173]. Patients with IBS-D may benefit of TCAs more than other subtypes[208,209].

SSRIs have been widely used for treatment of anxiety, depression, and somatisation disorders[210]. A few studies have assessed the role of SSRIs in IBS. Paroxetine improves QoL and overall well-being without a significant change in pain[211,212]. Fluoxetine may alleviate abdominal pain in patients with rectal hypersensitivity[213], and increase the frequency of bowel movements besides relieving pain in IBS-C[214]. According to a meta-analysis of five SSRI studies, NNT with SSRIs is 3.5 (95% CI 2 to 14)[207].

Alocetron, a 5-HT3 receptor antagonist, has high quality evidence from several studies on relieving global IBS symptoms in IBS-D with a NNT of 8. Due to serious side-effects, such as ischemic colitis and constipation-related surgery, however, it is not available in the EU market. The 5-HT4 partial agonist tegaserod is more efficient than a placebo in relieving global IBS symptoms in female patients with IBS-C or IBS-M. The proportion of responders is between 5 and 19% higher than with placebo in several studies. Due to a ten-fold risk (frequency 0.11%) of cardiovascular events compared to controls, however, the drug has been withdrawn from market.[181]

## Psychological therapies

Cognitive behavioural therapy[208,215,216], hypnotherapy[217,218], relaxation therapy (such as meditation)[219-221], stress management[222], multi-component psychological therapy[223,224], and dynamic psychotherapy[211,225] have been used to treat IBS. In a meta-analysis, the NNT of psychological studies was 4 (95% CI 3 to 5). Patients not responding to other IBS therapies could possibly benefit of psychological therapies, especially cognitive behavioural therapy. Most of the data is derived from small studies, however, and more large scale studies are needed to establish the role of psychological therapies in IBS.[207]

## Healthcare use

IBS symptoms are one of the most common reasons for physician visits in primary care and referrals to gastroenterologists[105,226]. In the US, functional GI disorders, such as constipation, dyspepsia, and IBS were among six leading GI physician diagnoses in outpatient visits in 2002[227]. Of those with IBS symptoms, 23 to 84% consult a primary care physician in a one year period[127,131,228-232]. According to some studies, females are up to 3.3 times more prone to seek healthcare for GI symptoms[105,233], while others have found no gender difference in consultation behaviour[77,229,231].

Severity and the number of GI symptoms, presence of comorbid conditions, psychological factors (such as coping ability), depression or anxiety, and reduced QoL have been shown to predict healthcare seeking[77,229,231,234-236]. Those with high levels of somatisation are more likely to be referred to secondary and tertiary centres[166] and they also exhibit more psychiatric symptoms and abnormal illness behaviour. In population surveys or patients with mild GI symptoms, however, the association of psychiatric symptoms and healthcare seeking seems to be weaker[237,238].

Besides consultations for GI symptoms, subjects with IBS make 2 to 3 times as many physician visits for non-GI reasons, and have increased rates of hospitalisations and surgical procedures[105,239,240].

In an Italian study, IBS-D was associated with an increased rate of physician visits [232]. In another study from US, however, no difference was detected in healthcare seeking behaviour between IBS subgroups[127].

### Abnormal illness behaviour

Besides multiple somatic complaints, inappropriate physician consultations for minor illnesses have been associated with IBS[241]. Illness behaviour refers to how a person perceives abnormal bodily signals, *i.e.* symptoms of a disease and how he or she acts upon them. The decision of consulting a physician depends on knowledge on various symptoms and possible diseases behind them, the perceived intensity of symptoms, and individual health concerns[235]. In IBS, normal visceral stimuli and bodily sensations can be misinterpreted as signs of a disease. Symptom severity, worry of a serious illness, anxiety, and depression has been shown to discriminate IBS consulters and non-consulters[242]. Also, beliefs about the efficacy of available treatments can influence consultation decisions. Finally, social support and individual coping skills can moderate healthcare seeking behaviour[234].

## Economic impact

The healthcare costs of IBS patients are more than 50% higher than controls[243,244]. IBS mostly affects working age people leading to productivity loss due to sick leave. In a study comparing IBS costs between the UK, Germany, Switzerland and Portugal, the total

annual costs varied between 700 and 1 600€ per subject[245]. In a population based study, annual direct costs were 860€ per patient in France[246]. Costs incurred by Rome II criteria are reported to be higher than those by Rome I[247].

The perspective of a cost evaluation may be that of an individual patient, a third-party payer (*i.e.* an insurance company or government), an individual hospital, or the society as a whole. In a societal perspective all expenditures are included regardless of the payer. Total expenditures consist of direct, indirect, and intangible costs. Direct costs are those related to use of healthcare services, medical investigations, and therapy. Indirect costs refer to productivity losses due to absenteeism from work and time spent at healthcare services. Intangible costs are incurred by pain, suffering, and reduced QoL, factors usually not evaluable in monetary terms.

## Direct costs

In a review of US and UK studies about the economic impact of IBS, direct annual costs ranged widely between $348 to $8750 per subject[248]. Comparison between studies is difficult because of calculation differences for mean costs per subject. Some authors include only those with nonzero charges (*i.e.* healthcare users)[243], others divide total costs by all participants even including non-healthcare users[246]. In addition, some only report GI related costs, while others include all costs irrespective of a particular diagnosis[243]. Different healthcare systems may also impede comparison. In a comparison between the UK and US, however, the use of healthcare facilities was largely similar despite differences in healthcare funding[249].

In the US, direct costs of IBS have been estimated at approximately $1.5 billion annually. In a comparison of 17 GI diseases in 1998, the highest direct costs were for GERD ($9.3 billion), followed by gallbladder disease, colorectal cancer, peptic ulcer, diverticular disease, pancreatic disease, non-foodborne diseases, and chronic liver diseases before IBS. Pharmaceutical costs were markedly higher for GERD ($5.9 billion) than IBS ($0.08 billion), accounting for the presence of few effective drugs for IBS. In IBS, office visits covered the largest share (17%) of directs costs, but only 6% in GERD.[250] Also in France, office visits formed the largest share of direct costs[246].

Hospital inpatient costs for IBS have shown a wide variation between studies. Some studies report equal costs for IBS and control groups[158,251], some higher for IBS[244,252], others lower for IBS group[253]. The share of hospital inpatient costs have ranged between 7 and 70% of direct IBS costs[254].

Diagnostic testing in IBS is performed to seek or rule out possible organic disease causing GI symptoms. In the US, almost one quarter of colonoscopies performed on patients under age 50, are for IBS symptoms[255]. A linear relationship has been detected between levels of somatisation and the amount of diagnostic testing for GI symptoms in IBS patients[256]. In a retrospective cohort analysis, colonoscopy or barium enema had been performed on 47% of patients with IBS[257].

## Indirect costs

Subjects with IBS incur indirect societal costs due to missed work days and impaired work performance because of GI symptoms. In a US bank employee study, IBS caused a reduction of 21% in work productivity, equivalent to working less than 4 days in a 5-day work week[258]. In another study, at least one third of IBS patients missed 1 working day monthly and 46% of them reported impairment at work because of GI symptoms[249]. IBS-employees with impaired work performance have more non-GI comorbidities, such as fibromyalgia, chronic fatique syndrome, and urinary tract symptoms, than those with normal work performance despite IBS[259].

# 3. AIMS OF THE STUDY

The main objectives of this thesis were:

1. To assess the prevalence of IBS
    a. To evaluate IBS prevalence according to a variety of IBS definitions and diagnostic criteria
    b. To assess the differences in symptom severity and health care use between subjects meeting differing IBS criteria
2. To evaluate the comorbidity in IBS and its impact on health care use
3. To investigate the connection of depressive and GI symptoms in the general population
4. To evaluate the societal costs of IBS

# 4. MATERIALS AND METHODS

## Sample

The study was a two-phase postal survey (Figure 2). A random sample of non-institutionalised persons aged 18 to 64, was drawn from the National Population Registry. It comprised 2 490 men and 2 510 women with subjects' name, address, postal code, and age.

Only subjects, whose mother tongue was Finnish, were sampled. Those living in the Ahvenanmaa communal area were not included, as 93% of its inhabitants had Swedish as their mother tongue at the time of the study.

The sample size of 5 000 subjects was based on an assumption of 10% IBS prevalence in the population according to previous studies in Western countries, and a response rate of 70% (3 500 questionnaires for analysis). This allows subgroup analyses in the IBS group to detect a 5 to 10% unit frequency difference of a variable between an IBS group and non-IBS group with 5% precision and 90% confidence.

## Questionnaires

### Questionnaire I (Appendix A)

Questionnaire I, which was sent to a random sample of 5 000 subjects, contained 58 items: basic demographics (age, gender, marital status, education, and working hours), presence of a variety of somatic conditions diagnosed by a physician (lactose intolerance, celiac disease, atopic diseases, or bronchial asthma). In addition, a history of abdominal surgery, abdominal pain during childhood, history of upper or lower GI endoscopy, presence of any chronic medical condition, and regular medication were inquired (see Appendix A).

Items covering IBS diagnostic questions and those related to severity of abdominal symptoms were translated into Finnish from the Rome II Integrative Questionnaire, covering functional GI disorders from oesophagus to anorectum, designed primarily for epidemiological surveys[19]. According to the coding instructions, detection of the Rome II IBS criteria is based on six items including a question on the frequency of abdominal pain (q17), pain improvement with defecation (q20), questions on frequency of bowel movements (q21-22) and a change in stool form (q23-24) associated with abdominal pain. In addition, the Rome II Questionnaire includes nine items covering IBS supporting symptoms: abnormal frequency of bowel movements (q30-31), abnormal form of stools (q32-33), feeling of incomplete evacuation (q34), straining during a bowel movement (q35), urgency (q36), passage of mucus (q37), and abdominal bloating (q38). These symptoms are used to subclassify IBS into constipation-predominant and diarrhoea-predominant patterns[19]. They also allow IBS detection according to the

Manning and Rome I criteria (Table 1). In the Questionnaire I, Manning 2 criteria were defined as fulfilment of at least two of the six Manning symptoms and presence of abdominal pain more often than one day out of ten during the previous year. In Manning 3 criteria, at least three Manning symptoms were required. Rome I criteria were defined as a combination of abdominal pain more often than one day out of four, pain eased after bowel movement or associated with a change in bowel habits, and at least two of the five IBS supporting symptoms[81] (Table 1). Dyspepsia was defined as presence of abdominal pain or discomfort (q17), localised in upper abdomen (q27-28), and not relieved with defecation (q20-24).

The response scale for all items to identify IBS and dyspepsia, as well as an item assessing the frequency of daily activities disturbed by pain, was a five grade frequency scale, which has later been proven to perform better than a binary scale[260]. Answering options were: 1) not at all or rarely; 2) occasionally; 3) often; 4) very often; 5) almost always. Time scales were defined as follows: *Occasionally:* more than one tenth of the time; *Often:* more than one quarter of the time; *Very Often:* more than one half of the time[19]. The severity of abdominal pain and discomfort during the previous year was assessed by the 4-grade Likert scale (mild, moderate, severe, and very severe).

The items translated into Finnish were then back-translated into English by an American-English translator. The back-translated items were compared with the original ones. Minor differences were noticed in the choice and order of words; such as "not at all or rarely" in the original was turned into "seldom or never" in the cross-translation. The cut-off points (choices such as "often") in the frequency scale were identical in both questionnaires, however, suggesting that translation of the questionnaire into Finnish would not affect the number of IBS subjects identified.

Response options for questions covering the number of physician visits for GI and non-GI symptoms during the previous year were: 1) none; 2) one to two times; 3) three to five times; 4) six to ten times; 5) more than ten times. To approximate the average number of physician visits, they were later recoded as: 0, 1.5, 4, 8, and 11. Sick leave days during the previous year were assessed by five choices: 1) none; 2) one to three days; 3) four to six days; 4) seven to twenty days; 5) more than twenty days; 6) not employed. To approximate the mean number of sick leave days, these choices were recoded as: 0, 2, 5, 10, and 22.

Frequency of taking prescription medication and over-the-counter medication for GI symptoms was assessed by five options: 1) not at all; 2) less than once a month; 3) on average one to three times a month; 4) on average one to three times a week; 5) daily or almost daily.

Frequency of headaches and back pain were inquired by four options: 1) less than once a month; 2) on average one to three times a month; 3) on average one to three times a week; 4) daily or almost daily.

The final section of Questionnaire I consisted of a Finnish version of the 13-item Beck's Depression Inventory Short Form (BDI-SF)[261-264]. The Finnish version (R-BDI-SF) includes 14 items: 13 for depressive symptoms and 1 for anxiety. It has been applied in population screening among Finnish adults and adolescents[265,266] and has shown a good correlation with the original 21-item Beck Depression Inventory[267]. R-BDI-SF

score ranges from 0 to 36. Depressive symptoms are graded as mild (score 5-7), moderate (score 8-15), or severe (score 16 or more). Anxiety is scored as mild (score 1), moderate (score 2), or severe (score 3)[264].

## Pilot study

To assess the acceptability and item selection of the seven-page Questionnaire I, we conducted a pilot study in August 2001. The questionnaire with an explanatory letter was given to 30 consecutive outpatients (17 women, 13 men) visiting a gastroenterologist in the Department of Gastroenterology, Helsinki University Central Hospital. The patients displayed a variety of gastrointestinal disorders: functional GI disorders, inflammatory bowel diseases, and hepatic diseases. They were asked to fill in the questionnaire in the waiting room before or after the doctor´s appointment and were encouraged to give comments on the questionnaire regarding the amount of items, contents of the questions, understanding of the questions, and suggestions for improving the questionnaire. Twenty-five patients returned the questionnaire. Completion of the questionnaire took approximately 12 minutes, which was regarded as a reasonable time by the patients. The questions were generally regarded as comprehensible and no changes were made to the questionnaire after the pilot study.

## Questionnaire II (Appendix B)

Questionnaire II, which was sent to those fulfilling IBS criteria in Questionnaire I, included detailed questions on the duration of GI symptoms, the most bothersome symptoms, and location of abdominal pain. GI-related healthcare use was assessed by questions on the number of physician visits at various levels of healthcare organisation (primary care, occupational health care, secondary care, emergency room, private sector). In addition, the number of upper GI endoscopies, colonoscopies, barium enema, and abdominal ultrasound ever performed, were inquired, as well as consumption of medication for GI symptoms within nine pharmacological groups (antacids, histamine-2-receptor blockers, proton-pump inhibitors, pain killers [including non-steroidal anti-inflammatory drugs and paracetamol], antidiarrhoeals, laxatives, fibre products, antispasmodics, and prokinetics) during the previous three months. In addition, family history of inflammatory bowel disease, colorectal cancer, and celiac disease was inquired, (see Appendix B).

The number of physician visits during the previous year was inquired by six options: 1) none; 2) once; 3) twice; 4) three times; 5) four to six times; 6) more than six times. To approximate the average number of visits, “four to six times” was recoded as “five”, and “more than six times” as “seven”.

For use of medication, the answering options were: 1) not at all; 2) less than twice a month; 3) two to three times a month; 4) one to two times a week; 5) three to five times a

week; 6) daily or almost daily. To approximate the mean monthly use of medication these options were recoded as 0; 1; 2.5; 6; 16, and 24.

The final part of the Questionnaire II consisted of a validated Finnish version of the RAND 36-Item Health Survey 1.0, a generic health-related QoL measurement tool[268].

For estimating the direct and indirect IBS costs, a societal perspective was obtained, *i.e.* all costs were taken into account regardless of the payer. Direct costs included those for physician visits, transportations, GI endoscopies, and medication. Indirect costs included expenses due to sick leave and time costs of physician visits and endoscopies.

The unit costs for physician visits, transportation, and time costs were derived from the National Research and Development Centre for Welfare and Health[269]. Costs of GI endoscopies were calculated as average prices between five university hospital districts of Finland. Medication costs were calculated based on a defined daily dose weighted with unit sales records within the ATC-4 group. Retail prices without VAT were derived from pharmacist price lists. Sick leave expenses, applying the human capital method[270], were valued as average of lost earnings obtained from Statistics Finland[271].

## Data collection

Questionnaire I was sent on the 18th of September 2001. The first reminder for non-respondents was sent on the 30th of October, and the final reminder on the 12th of December 2001.

Questionnaire II was sent to 591 subjects who met IBS criteria either by Manning $\geq 2$ symptoms, or Rome II criteria in Questionnaire I. First mailing was on the 20th of February 2002. For non-responders, two reminders were sent 6 weeks apart.

All returned questionnaires were optically scanned and the data transformed into an Excel form. Statistical analyses were performed with NCSS-2000 software for Windows (NCSS Statistical Software, Kaysville, UT) and SPSS 13 software for Windows (SPSS, Inc, Chicago, IL, USA).

## Control groups

In study I, four partially overlapping IBS groups were formed (Manning 2, Manning 3, Rome I, and Rome II). Non-IBS controls were subjects who did not meet the IBS criterion in question regardless of the possible reporting of GI symptoms and meeting another of the four IBS criteria.

In study II, IBS was defined as those fulfilling the Rome II IBS criteria. The control group included all subjects not meeting Rome II criteria.

In study III, frequencies of GI symptoms were compared between subjects reporting depressive symptoms and non-depressive controls. The control group was defined as subjects with an R-BDI-SF score of less than five.

In study IV, IBS related costs were compared between subjects fulfilling Rome II criteria and Manning 2 criteria. The control group consisted of those subjects fulfilling neither Rome II nor Manning 2 criteria.

## Statistical methods

Prevalence figures for categorical variables were calculated with 95% confidence intervals (CI). Due to overlap of the four IBS criteria, 95% CIs were applied for comparison of frequencies of binary variables between the groups. Differences were considered statistically significant, if their 95% CIs did not overlap. Direct adjustment against Finnish population aged 18 to 64 was applied for age and gender adjustment of the prevalence figures by various IBS criteria and depressive symptoms.

In study I, concordance between different diagnostic criteria was calculated applying kappa-statistics (κ). A κ-value of 0.0 to 0.2 indicates slight agreement, 0.2 to 0.4 fair agreement, 0.4 to 0.6 moderate agreement, 0.6 to 0.8 substantial agreement, and a κ-value of 0.8 to 1.0 near perfect agreement[272].

Several variables with multiple categories, such as marital status, basic education, working hours, depression score, and anxiety, were dichotomized for comparison. The chi-square test was applied for categorical and T-test for dimensional variables. In study II, the Bonferroni correction for multiple testing was applied. For nonparametric comparison of medians, the Mann-Whitney's U-test was applied between two-group testing, and Kruskall Wallis test between three groups.

In study II, the distribution of comorbid conditions was compared between GI consulters and non-consulters among IBS group and controls. GI-consulters referred to those with at least one physician visit for GI symptoms during the previous year. A loglinear model was applied for comparison of categorical variables, and a two-way analysis of variance for continuous variables. To detect independent predictors of healthcare seeking for GI and non-GI reasons, a stepwise logistic regression analysis was performed with 26 variables: fixed variables (IBS, age, gender, basic education), working hours, employment status, marital status, GI conditions (dyspepsia, diarrhoea, constipation, severe abdominal pain, disturbance of daily activities because of GI symptoms, lactose intolerance, celiac disease, history of abdominal pain during childhood, history of abdominal surgery), allergic conditions (asthma, food allergy, allergic dermatitis, allergic rhinitis), other extra-GI conditions (headache, back pain, chronic medical condition), and psychiatric conditions (depression, anxiety and insomnia). In addition, interaction variables of each comorbid condition and IBS were generated and included in the regression model. For non-GI reasons, a majority of subjects in both the IBS and control groups had made at least one consultation during the previous year. Therefore, a consulter was defined as a subject with at least three non-GI visits.

In study III, independent factors associated with depressive symptoms were generated with a stepwise logistic regression analysis. Altogether 14 variables were included in the model: age, gender, educational level, marital status, employment status, working hours,

chronic medical condition, anxiety, IBS, dyspepsia, diarrhoea, constipation, frequent abdominal pain, and history of abdominal surgery.

In study IV, the non-parametric bootstrap technique[273] was applied for comparison of the skewed cost data. The number of bootstrap replications was 10 000 and 95% confidence intervals were constructed by bootstrap percentile method where the lower and upper limits of the confidence interval are the 0.025 and 0.975 quantiles of the bootstrap distribution. The p-values for the differences between means were constructed by a randomisation test. The number of permutations in the tests was 10 000.

All p-values calculated were two-tailed. A p-value of less than 0.05 was considered statistically significant.

## Ethics

The Ethics Committee of the Helsinki University Hospital evaluated the study protocol and stated that no ethical considerations by the committee are needed as the study is a postal survey.

# 5. RESULTS

For Questionnaire I, 5 000 letters were sent. Due to unknown addresses, 22 were returned. After two reminders, a total of 3 631 subjects participated in the study by returning the Questionnaire. A total of 20 questionnaires were returned unfilled. Questionnaire II was sent to 591 subjects fulfilling the Manning or Rome II IBS criteria in Questionnaire I. Of Phase II questionnaires, 8 went to unknown addresses. Altogether 499 filled and two unfilled questionnaires were returned (Figure 2).

The overall response rate for Questionnaire I was 73%. It was higher among females than males (79% vs. 67%). Mean respondent age was 42.1 years (95% CI 41.6-42.5), and non-respondents 38.7 years (95% CI 37.3-39.0). Of respondents, 55% were females (female to male ratio 1.2:1), whereas 39% of non-respondents were females. Among both male and female respondents, the youngest age group (18-24 years) was under-represented and oldest age group (55-64 years) over-represented (Table 2).

For Questionnaire II, the overall response rate was 86% (n=501). No gender difference emerged in any of the age groups. Mean respondent and non-respondent age was 42.2 (95% CI 41.1-43.4) and 37.4 (95% CI 35.0-40.0) years. The proportion of females among respondents and non-respondents was 64% and 66% (p = 0.781).

**Table 2**. Response rate (%)

| Age (years) | Questionnaire I | | | | Questionnaire II | | | |
|---|---|---|---|---|---|---|---|---|
| | Male n=1 639 | Female n=1 991 | Total n=3 631 | p* | Male n=179 | Female n=322 | Total n=501 | p* |
| 18-24 | 53.5 | 73.5 | 63.3 | <0.000 | 81.0 | 88.0 | 85.9 | 0.436 |
| 25-34 | 67.1 | 76.2 | 71.6 | 0.002 | 82.5 | 77.9 | 79.5 | 0.338 |
| 35-44 | 62.6 | 78.7 | 70.6 | <0.000 | 76.0 | 84.8 | 81.7 | 0.196 |
| 45-54 | 69.5 | 79.5 | 74.6 | <0.000 | 94.7 | 87.4 | 90.3 | 0.144 |
| 55-65 | 81.1 | 85.0 | 83.1 | 0.124 | 94.9 | 91.4 | 92.7 | 0.509 |
| Total | 67.0 | 78.9 | 72.9 | <0.000 | 86.5 | 85.6 | 85.9 | 0.781 |

*Male vs. female

n = number of respondents

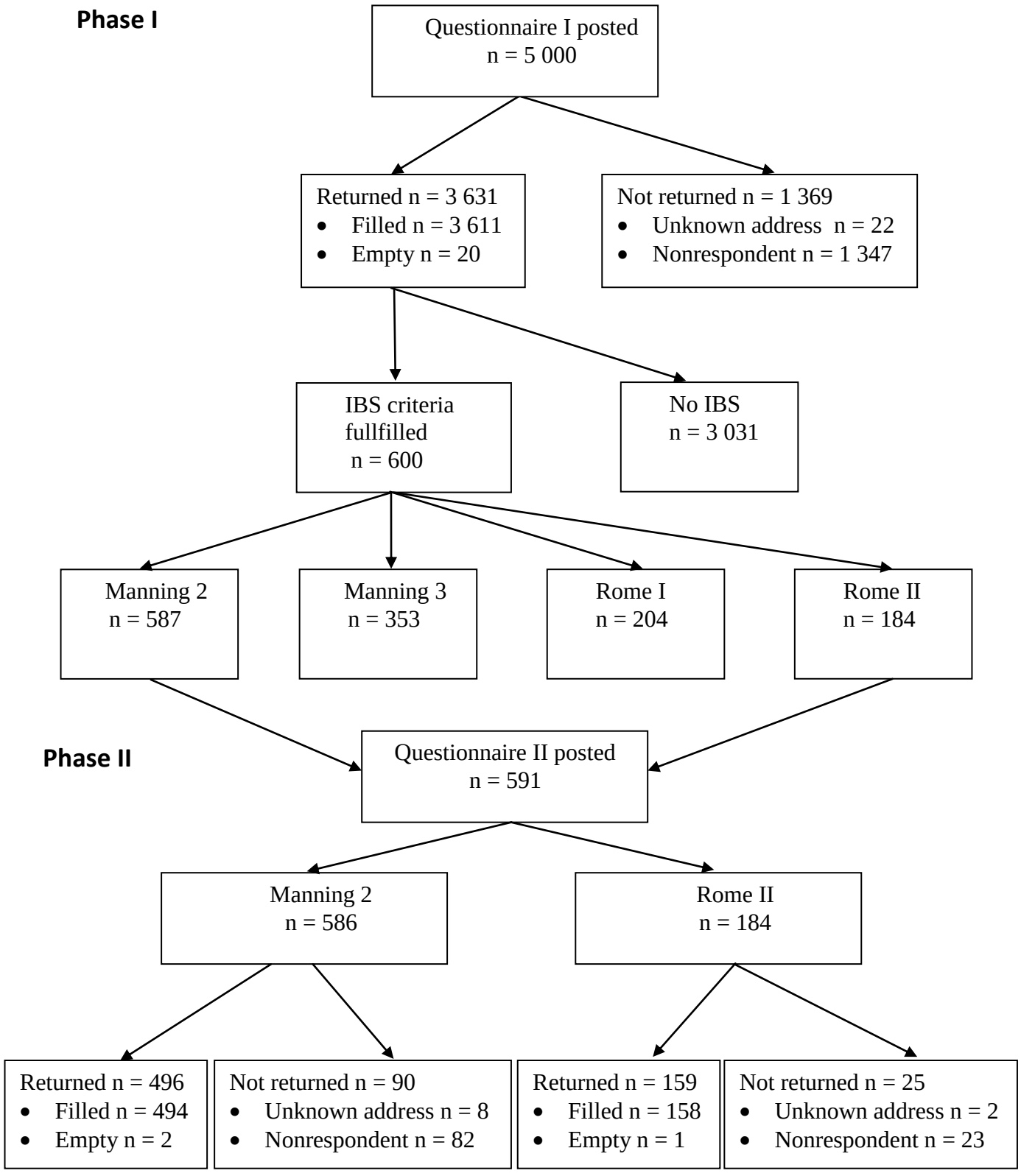


**Figure 2.** Flow chart of the study. Manning 2, at least two Manning symptoms; Manning 3, at least three Manning symptoms.

## Prevalence of IBS (I)

At least one of the four IBS criteria was met by 600 subjects, which accounted for 16.5% of the respondents. The female to male ratio was 1.8:1. Manning 2 criteria represented the broadest IBS definition with a crude prevalence of 16.2% (95% CI 15.0-17.4%). After adjusting for age and gender, the prevalence was 15.9% (95% CI 14.7-17.1%). The most stringent criteria were Rome II, with a total of 184 respondents. Crude IBS prevalence was 5.1% (95% CI 4.4-5.8%). After adjusting for age and gender, the prevalence figure remained the same.

A significant gender difference appeared in both the Manning 2 and Manning 3 groups, with female to male ratio of 1.5:1 and 1.4:1, respectively. In Rome I and Rome II groups, no gender difference was evident (Table 3).

**Table 3.** Prevalence of IBS according to varying diagnostic criteria (%, 95% CI)

| | Manning2 (n=587) | Manning3 (n=353) | Rome I (n=201) | Rome II (n=184) |
|---|---|---|---|---|
| Crude | | | | |
| Total | 16.2 (15.0-17.4) | 9.7 (8.8-10.7) | 5.5 (4.8-6.3) | 5.1 (4.4-5.8) |
| Male | 13.1 (11.4-14.8) | 8.3 (7.0-9.7) | 5.1 (4.0-6.2) | 5.1 (4.0-6.2) |
| Female | 19.2 (17.4-20.9) | 11.2 (9.8-12.6) | 6.1 (5.0-7.2) | 5.3 (4.3-6.3) |
| Adjusted | | | | |
| Total | 15.9 (14.7-17.1) | 9.6 (8.6-10.6) | 5.6 (4.8-6.4) | 5.1 (4.4-5.8) |
| Male | 12.8 (11.1-14.4) | 8.1 (6.7-9.5) | 4.9 (3.8-6.0) | 4.9 (3.8-6.0) |
| Female | 19.1 (17.3-20.9) | 11.2 (9.8-12.6) | 6.2 (5.1-7.3) | 5.2 (4.2-6.2) |

In Manning 2 and 3 groups, the prevalence of IBS showed a declining tendency, although not statistically significant, from age 35 upwards (Table 4).

**Table 4**. Fulfillment of varying IBS criteria according to age (%, 95% CI).

| | Manning2 (n=587) | Manning3 (n=353) | Rome I (n=201) | Rome II (n=184) |
|---|---|---|---|---|
| Age 18-24 (n=416) | 17.8 (14.1-21.5) | 10.3 (7.4-13.3) | 6.0 (3.9-8.8) | 5.3 (3.3-7.9) |
| Age 25-34 (n=683) | 17.4 (14.6-20.3) | 10.5 (8.2-12.8) | 5.3 (3.7-7.2) | 5.3 (3.7-7.2) |
| Age 35-44 (n=837) | 16.7 (14.2-19.3) | 9.7 (7.8-11.9) | 5.6 (4.2-7.4) | 4.9 (3.5-6.6) |
| Age 45-54 (n=941) | 15.4 (13.1-17.7) | 9.8 (8.0-11.9) | 5.7 (4.3-7.4) | 4.8 (3.5-6.3) |
| Age 55-65 (n=753) | 14.5 (12.0-17.0) | 8.6 (6.7-10.9) | 5.6 (4.1-7.5) | 5.3 (3.8-7.2) |
| p ($\chi$2 test) | 0.445 | 0.776 | 0.991 | 0.982 |

The mean age for those fulfilling an IBS criterion did not differ from those not fulfilling. In addition, no difference was detected regarding marital status. In both Manning groups, a lower proportion of subjects had primary school or less as their basic education compared to those not fulfilling Manning criteria. No differences in basic education appeared in the Rome groups. In the Manning 3 group, a larger share had irregular working hours than those not fulfilling Manning 3 criteria.

Regardless of criteria applied, the diarrhoea-predominant subtype was the most common covering 41 to 57% of subjects fulfilling any IBS criterion. The proportion of constipation-predominant subtype ranged between 16 and 27%. In Rome II group, frequency of constipation did not differ from that of the total sample (Table 6.)

## Overlap of IBS criteria (I)

A substantial overlap between various IBS criteria was detected. Manning 2 criteria was met by 97% of those fulfilling Rome II criteria. Only four subjects (2.2%) in the Rome II group exclusively met Rome II criteria (Table 5). Manning 2 criteria showed a substantial agreement with Rome I and Rome II criteria, with kappa-values of 0.45 and 0.42. Manning 3 criteria's agreement with Rome I and Rome II was slightly better, kappa-values were 0.53 and 0.52. A substantial agreement (kappa-value 0.78) was detected between Rome I and Rome II criteria.

**Table 5**. Overlap between diagnostic criteria. Number and percentage of subjects in column group also meeting upper row criteria.

| | M2 | | M3 | | RI | | RII | | Only Column criteria | |
|---|---|---|---|---|---|---|---|---|---|---|
| | n | % | n | % | n | % | n | % | n | % |
| M2 | 587 | 100 | 0 | 0 | 195 | 33 | 179 | 30 | 183 | 31 |
| M3 | 0 | 0 | 353 | 100 | 157 | 44 | 149 | 42 | 182 | 52 |
| RI | 195 | 96 | 157 | 77 | 204 | 100 | 153 | 75 | 8 | 4 |
| RII | 179 | 97 | 149 | 81 | 153 | 83 | 184 | 100 | 4 | 2.2 |

**Table 6**. Sociodemographic and symptom charasteristics of total sample and each IBS criterion

| | Total sample (n = 3 631) | Manning2 (n = 587) | p† | Manning3 (n = 353) | p† | Rome I (n = 204) | p† | Rome II (n = 184) | p† |
|---|---|---|---|---|---|---|---|---|---|
| Gender, n (%) | | | p1** | | p1* | | p1 = 0.108 | | p1 = 0.640 |
| Male | 1 639 (45.2) | 209 (35.6) | | 132 (37.4) | | 81 (39.7) | | 80 (43.5) | |
| Female | 1 991 (54.8) | 378 (64.4) | | 221 (62.6) | | 123 (60.3) | | 104 (56.5) | |
| Mean age, years (SD) | 42.3 (12.8) | 41.4 (12.9) | 0.066 | 41.5 (12.7) | 0.239 | 42.5 (12.9) | 0.844 | 42.2 (13.1) | 0.888 |
| Marital status, n (%) | | | | | | | | | |
| Married or common law marriage | 2 411 (67.1) | 398 (67.8) | 0.686 | 248 (68.6) | 0.536 | 138 (67.6) | 0.860 | 120 (65.2) | 0.580 |
| Basic education, n (%) | | | | | | | | | |
| Primary school or less | 863 (24.1) | 112 (19.2) | * | 67 (19.1) | 0.020 | 48 (23.6) | 0.867 | 40 (22.0) | 0.486 |
| High school graduate | 1 182 (33.1) | 192 (32.9) | 0.921 | 119 (33.9) | 0.722 | 55 (27.1) | 0.063 | 50 (27.5) | 0.100 |
| Irregular working hours, n (%) | 751 (21.2) | 138 (24.0) | 0.074 | 90 (26.1) | 0.019 | 53 (26.6) | 0.053 | 45 (25.1) | 0.183 |
| Diarrhoea, n (%) | 521 (14.3) | 242 (41.2) | ** | 168 (47.6) | ** | 110 (53.9) | ** | 104 (56.5) | ** |
| Constipation, n (%) | 548 (15.1) | 133 (22.7) | ** | 66 (18.7) | 0.046 | 54 (26.5) | ** | 30 (16.3) | 0.63736 |
| Dyspeptic symptoms, n (%) | 288 (7.9) | 172 (29.3) | ** | 107 (30.3) | ** | 98 (48.0) | ** | 83 (45.1) | ** |
| Lactose intolerance, n (%) | 344 (9.6) | 129 (22.2) | ** | 70 (19.9) | ** | 53 (26.1) | ** | 44 (24.3) | ** |
| Abdominal pain in childhood, n (%) | 393 (11.1) | 137 (23.8) | ** | 89 (25.8) | ** | 68 (34.0) | ** | 61 (33.3) | ** |
| Allergic condition, n (%) | 626 (18.1) | 128 (23.0) | ** | 83 (24.6) | * | 40 (20.8) | 0.314 | 43 (24.9) | 0.018 |
| Asthma, n (%) | 122 (3.5) | 33 (5.8) | 0.001 | 22 (6.4) | 0.002 | 10 (5.0) | 0.224 | 14 (7.8) | 0.001 |
| Headache, n (%) | 370 (10.3) | 123 (21.0) | ** | 82 (23.3) | ** | 54 (26.6) | ** | 50 (27.3) | ** |
| Back pain, n (%) | 568 (15.9) | 173 (29.6) | ** | 113 (32.2) | ** | 80 (39.6) | ** | 64 (35.0) | ** |
| Depressive symptoms, n (%) | 602 (17.0) | 175 (30.5) | ** | 120 (34.8) | ** | 84 (42.9) | ** | 70 (39.3) | ** |
| Anxiety, n (%) | 817 (22.8) | 229 (39.4) | ** | 139 (39.6) | ** | 92 (45.3) | ** | 77 (42.1) | ** |
| Insomnia, n (%) | 630 (17.5) | 155 (26.5) | ** | 98 (27.8) | ** | 66 (32.4) | ** | 59 (32.1) | ** |

†p-value vs. those not meeting the criterion

p1-value male vs. female

* < 0.01

** < 0.0001

## GI symptom severity (I)

Presence of severe or very severe abdominal pain was reported by 44% (95% CI 36.6-51.1), 45% (95% CI 38.0-51.9), 30% (95% CI 25.2-34.8), and 27% (95% CI 23.7-30.9) of subjects in Rome II, Rome I, Manning 3, and Manning 2 groups. Daily activities were disturbed by abdominal pain often or very often by 64% (95% CI 57.2-71.1), 65% (95% CI 58.5-71.6), 33% (95% CI 27.9-37.7), and 29% (95% CI 25.3-32.6) of subjects in Rome II, Rome I, Manning 3, and Manning 2 groups (see Study I, Figure 2).

## Prevalence of depressive symptoms (III)

According to R-BDI-SF, a total of 602 participants reported depressive symptoms corresponding to 17.0% (95% CI 15.7-18.2%) of the total sample, with no gender difference. Due to incompletely filled R-BDI-SF, depression score could not be rated for 82 subjects, who were excluded from the analysis. After age and gender adjustment, the prevalence of depressive symptoms was 16.7% (95% CI 15.4-17.9%). Independent predictors of depressive symptoms were anxiety, frequent abdominal pain (pain more often than 1 day of 4), diarrhoea, constipation, and a chronic medical condition. Higher basic education and marriage or cohabiting with a partner protected against depressive symptoms (see Study III, Table 2).

Of subjects with depressive symptoms, 11.6% (95% CI 9.1-14.2%) fulfilled Rome II IBS criteria, compared to only 3.7% (95% CI 3.0-4.4%) of the non-depressive control subjects. In addition, diarrhoea, constipation, and dyspepsia rates were higher amongst subjects with depressive symptoms.

## Comorbidity in IBS (I,II)

Rates of dyspeptic symptoms, lactose intolerance, headache, back pain, depression, anxiety, and insomnia were higher for subjects meeting any IBS criterion than for controls. In addition, they had more often experienced abdominal pain during childhood. Presence of asthma or an allergic condition (food allergy, allergic dermatitis, or allergic rhinitis) was reported more often than controls in both Manning groups and the Rome II group, but no excess rates were reported in the Rome I group (Table 6).

Prevalence of depressive symptoms (depression score 5 or more according to R-BDI-SF) in the Rome II, Rome I, Manning 3, and Manning 2 groups was 39% (95% CI 32.1-46.5%), 43% (95% CI 35.9-49.8%), 35% (95% CI 29.8-39.8%), and 31% (95% CI 26.7-34.3%). Depressive symptoms were significantly more common in the Rome I group

than the Manning 2 group. In addition, anxiety and insomnia were more common amongst those meeting an IBS criterion than those not meeting it (Table 6).

## Healthcare use (I,II,IV)

During the previous year, a higher proportion of subjects fulfilling any IBS criterion had made physician visits for both GI and non-GI symptoms than the total sample. Compared to subjects fulfilling either of the Manning criteria, a larger proportion of those fulfilling either of the Rome criteria reported visiting physicians for GI symptom (Figure 3). No difference emerged in non-GI visits between IBS groups.

The mean number of GI visits was 0.8 (95% CI 0.7-0.9) and 1.5 (95% CI 1.1-1.8) in the Manning 2 and in Rome II groups. In the control group (those fulfilling neither Rome II nor Manning 2 criteria), subjects reported on average 0.23 (95% CI 0.20-0.26) GI visits during the previous year. For non-GI visits, subjects in the Manning 2 group reported on average 3.0 visits (95% CI 2.7-3.2) and those in the Rome II group 3.2 visits (95% CI 2.8-3.6). Subjects in the control group reported on average 2.3 (95% CI 2.2-2.3) non-GI visits during the previous year (IV).

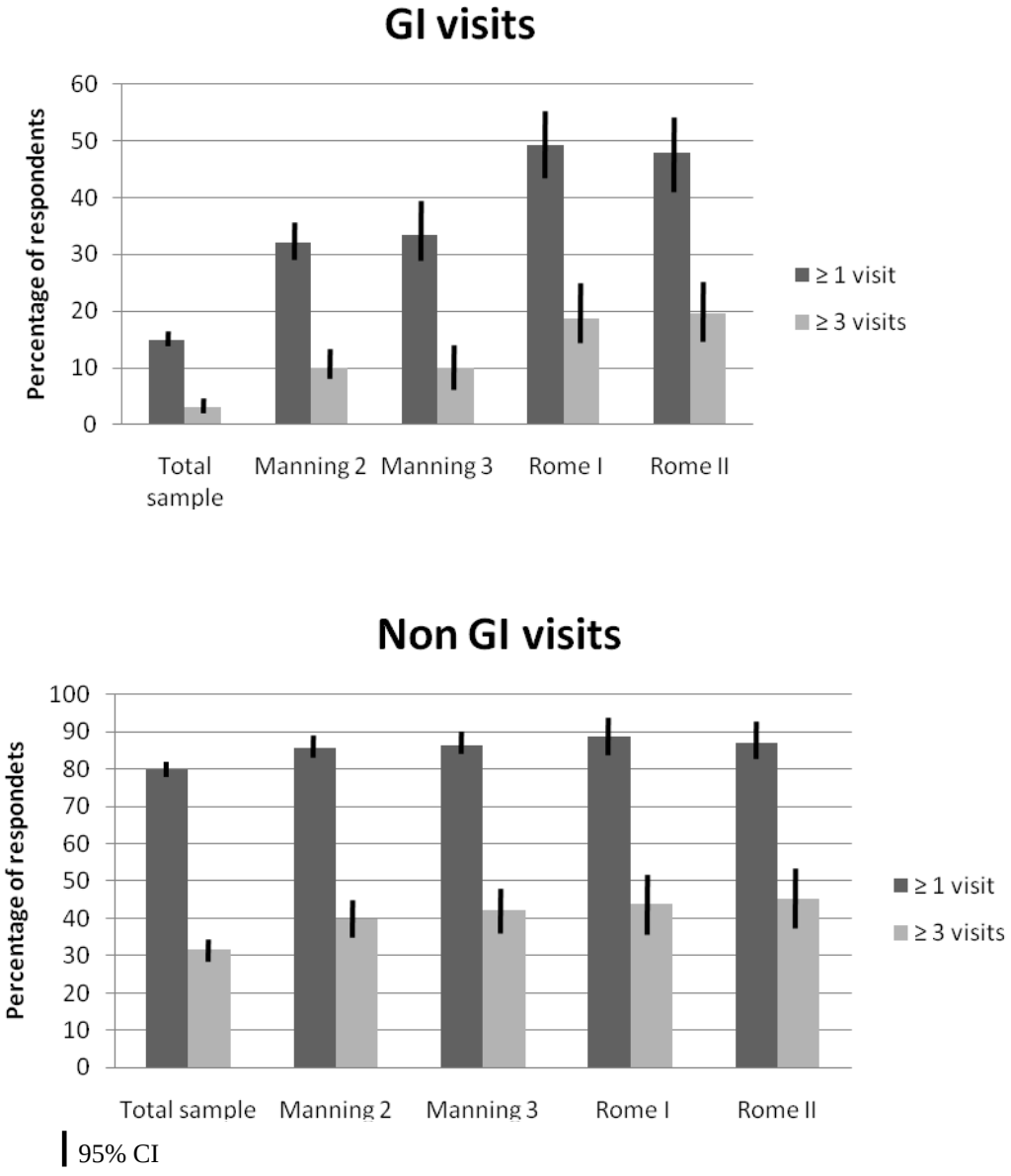


**Figure 3.** Visits to physicians for GI and non-GI reasons during the previous year.

### Predictors of healthcare seeking (II, III)

In study II we compared subjects fulfilling Rome II IBS criteria to controls. In the control group, rates of lactose intolerance, diarrhoea, food allergy and headache were higher among GI consulters (those with at least one physician visit for GI reasons) than among non-consulters. However, in the Rome II group, rates of these conditions were lower among GI consulters (see Study II, Table 1). In addition, in the control group, rates of

depressive symptoms and anxiety were higher for GI consulters, but no difference emerged in the Rome II group between GI consulters and non-consulters.

When comparing the rates of dyspepsia, extra-GI somatic symptoms (headache, back pain, allergic conditions), or psychiatric symptoms (depression, anxiety, insomnia) between GI consulters and non-consulters in the Rome II group, only dyspepsia was more common among GI consulters (Figure 4).

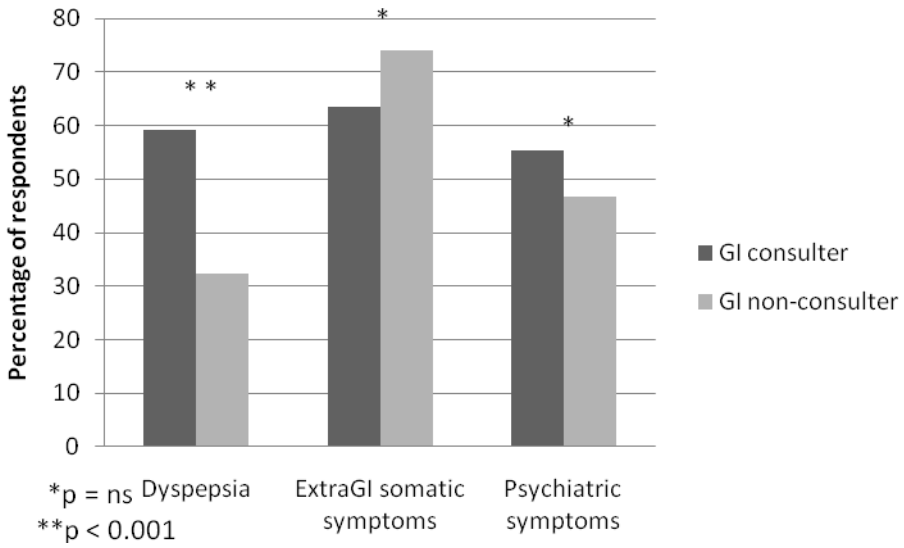


**Figure 4.** Rates of comorbid symptoms in Rome II group between GI consulters and non-consulters.

In the logistic regression analysis, the strongest independent predictors of GI visits were GI symptoms, such as disturbing abdominal symptoms (OR 4.06, 95% CI 2.74-6.01), severe abdominal pain (OR 2.56, 95% CI 1.74-3.79), and dyspeptic symptoms (OR 2.30, 95% CI 1.62-3.27). Of the non-GI symptoms in the regression model, only insomnia (OR 1.57, 95% CI 1.21-2.06), headache (OR 1.43, 95% CI 1.04-1.97), and chronic illness (1.39, 95% CI 1.08-1.78) predicted healthcare seeking for GI symptoms. Co-occurrence of IBS and the variables in the regression model did not increase the probability of consulting a physician.

Presence of chronic illness (OR 3.16, 95% CI 2.62-3.82), back pain (OR 2.01, 95% CI 1.61-2.51), and depressive symptoms (OR 1.79, 95% CI 1.37-2.10) were the strongest predictors of non-GI visits. Of the GI symptoms in the regression model, only presence of dyspeptic symptoms (OR 1.64, 95% CI 1.20-2.25) and a history of abdominal pain in childhood (OR 1.39, 95% CI 1.07-1.81), but not IBS, predicted non-GI visits (see study II, Table III).

### Depressive symptoms and health care seeking for GI reasons

In study III, GI related health care use was compared between subjects with depressive symptoms and non-depressive controls. At least one visit for GI reasons during the previous year was reported by 24% compared to 13% of controls ($p < 0.0001$). In addition, 18% of subjects with depressiveness had sick leave because of GI symptoms compared to 9% of controls ($p < 0.0001$).

## Societal costs (IV)

In study IV, annual societal costs were compared between subjects fulfilling Manning 2 and Rome II criteria. Total GI related costs per subject were higher in the Rome II group (497€, 95% CI 382-621€) than in the Manning 2 group (295€, 95% CI 246-347€, $p < 0.001$). When allowing for population prevalences according to each criterion, the nationwide annual GI related costs were higher by Manning criteria than by Rome II criteria (154M€, 95% CI 128-181M€ vs. 82M€, 95% CI 63-103M€).

Direct costs covered two thirds of the total GI costs. The single most expensive cost component was the share of physician visits, accounting for approximately 60 % (59% to 63%) of the direct costs and 40 % (40% to 42%) of the total GI related costs in IBS. The distribution of GI costs was nearly identical in Manning 2 and Rome II groups (Figure 5).

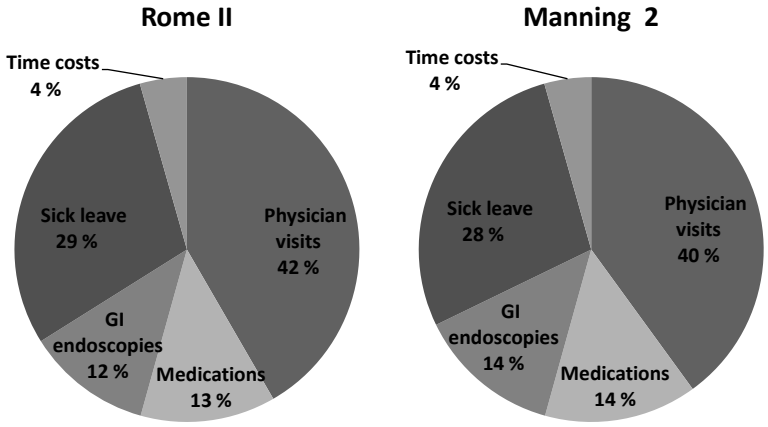


**Figure 5**. Distribution of GI expenses in Rome II and Manning 2 groups.

Subjects fulfilling either IBS criteria more often used GI medication than controls. The share of medications was 13% to 14% of the total GI costs. Acid controlling medication formed 74% to 78% of the drug costs. Of medications for lower GI symptoms, bulking agents incurred the highest expense, which was, however, only 5% to 7% of the drug

expenses. Medication expenses per subject were higher in the Rome II group (63€, 95% CI 44-86€) than in the Manning 2 group (42€, 95% CI 33-52€, $p < 0.001$). In the Manning 2 group, total drug expenses per subject were slightly higher among females than males (see study IV, Table 3).

Annual direct costs of GI endoscopies per subject were 40€ (95% CI 30-50€) in the Manning 2 group and 58€ (95% CI 39-81€) in the Rome II group ($p < 0.001$), with no gender difference. At least one colonoscopy was in the history of 46% (95% CI 38.0-53.7) of the subjects in the Rome II group and 32% (95% CI 28.0-36.4) in the Manning 2 group. For those with at least one colonoscopy performed, the average number of procedures was 1.6 (95% CI 1.3-1.8) in the Rome II group and 1.5 (95% CI 1.4-1.7) in the Manning 2 group.

For non-GI visits, the direct individual costs were 242€ (95% CI 223-260€), 262€ (95% CI 228-296€), and 184€ (95% CI 177-190€) in the Manning 2, Rome II, and control groups. Nationally, the direct non-GI visit costs amounted to 126M€ by Manning, and 43M€ by Rome II criteria. Direct GI and non-GI expenditures altogether ranged between 98 M€ by Rome II and 230 M€ by Manning criteria.

The average number of sick leave days per subject for GI symptoms was 0.9 (95% CI 0.7-1.2) and 1.8 (95% CI 1.0-2.6) in the Manning 2 and Rome II groups, while controls reported on average 0.3 (95% CI 0.2-0.4) days off work. No gender difference was evident in any group. Individual costs of these days were higher in the Rome II group (147€, 95% CI 88-214€) than in the Manning 2 group (82€, 95% CI 60-107€, $p < 0.001$), (see study IV, Table 4).

GI related costs were also assessed by duration of GI symptoms by three categories: symptom duration of less than three years, three to ten years, and more than ten years. No difference was detected in direct or indirect GI related costs between subjects with different symptom duration. In addition, age group had no effect on total costs.

# 6. DISCUSSION

The prevalence of IBS shows substantial variation depending on the applied diagnostic criteria. Of the four IBS criteria studied, both Rome criteria are more stringent than the older Manning criteria and they indentify an IBS population with more severe GI symptoms and more use of health care resources than those identified by the Manning criteria. IBS imposes a considerable burden for IBS sufferers and society. It is associated with high rates of psychiatric and somatic comorbidity and healthcare use for both GI and non-GI reasons. High population prevalence of IBS and increased use of healthcare resources incur high societal costs. Annually, individual GI related costs are almost twice as high by Rome II as Manning 2 criteria. Manning 2 criteria, however, identifies a three times larger IBS group owing to almost double the total societal GI related costs in Finland compared to Rome II criteria.

## Methodological aspects

Our study was a large scale population based survey with high response rates lending support to the findings. A population based approach enables inclusion of subjects not using healthcare services. The Rome II Integrative Questionnaire is designed for epidemiological surveys, and R-BDI –SF, validated in Finnish[267], has been widely used in surveys for detecting depressive symptoms.

As the Rome II Questionnaire was not available in Finnish, we translated the items used in our study. Translation may produce a source bias as the meaning of some expressions may differ between languages and cultures. Back-translation of the Questionnaire did not, however, reveal such biases suggesting that the translation process did not affect the number of identified IBS subjects.

For Questionnaire I, females were more prone to respond and consequently female to male ratio in the final data was 1.22:1, while at the time of the study, the ratio was 0.98:1 among Finnish inhabitants of age 18 to 64 years. Although the response rate was good overall, only 53.5% of males in the youngest age group responded possibly biasing results concerning them. The responders were on average 3.4 years older than non-responders which probably does not affect the results as the difference is considerably small and the total costs in the study were not higher for subjects in the oldest age groups.

No formal diagnoses of IBS or depression were confirmed by a physician as the study was a postal survey. Therefore, it is possible that some subjects fulfilling IBS criteria had an organic disease explaining GI symptoms. In the general population, however, functional bowel disorders are much more prevalent than organic diseases causing IBS-like symptoms[9]. Therefore, we assume that the IBS prevalence rates detected by our questionnaire are not significantly biased by organic diseases in the population. Although the BDI-SF is a self-reported depression symptom-rating scale and cannot substitute a diagnostic interview, it has shown a good correlation with moderate and severe depression in medical in-patients[274].

In Questionnaire I, the average number of physician visits and work absenteeism days due to GI symptoms were estimated based on five-scale categorised items, which may bias the cost estimation of non-GI visits and the number of sick leave days. In Questionnaire II, the six-scale categorised items on GI visits offer more exact data as only three subjects in the Manning group and two in the Rome II group reported more than six GI visits.

## Comparison of IBS criteria

In previous literature, the comparison of prevalence estimates and economic burden of IBS between individual countries and studies has been hampered by differences in IBS definition and criteria. In addition, composition of study population, research methodology, and sampling methods vary between studies. In our study, a substantial variation in the prevalence rates of IBS was seen depending on the applied diagnostic criteria, in line with two previous studies applying various IBS criteria on a population sample[75,76]. Even when applying the same study methodology across eight European countries, however, a two-fold variation has been detected in IBS rates suggesting that true prevalence variations exist between individual countries, associated possibly with cultural and dietary habits[92].

In this study, a three-fold difference in IBS prevalence rates was detected between the four IBS criteria. Manning 2 criteria were the most liberal and Rome II the most stringent. Two previous studies comparing Manning 2 and Rome II criteria obtained two to three-fold prevalence figures, in line with our results[75,130]. In a systematic review targeting US population based studies applying only Rome definitions, IBS prevalence was in the same order as ours ranging between 5 to 10% with a pooled prevalence of 7% (95% CI 6-8%)[275].

In our study, almost all subjects fulfilling Rome II criteria also fulfilled Manning 2 criteria. They formed a virtual subgroup of Manning 2 group with more severe abdominal pain, more disturbances of daily activities from symptoms, more use of healthcare services, and higher GI symptom related costs than those identified by just Manning criteria. This finding can partly be explained by the lesser requirement of pain in Manning criteria. Of the six Manning symptoms, only three are related to pain (looser stools at onset of pain, more frequent bowel movements at onset of pain, and pain eased after bowel movement). Abdominal pain disturbs daily activities and it predicts the use of the healthcare system which incurs economic expenses. According to the coding system in the Rome II Integrative Questionnaire, the required frequency of abdominal pain or discomfort to fulfil the criteria is “often”, which means more frequently than one day out of four. In the original Rome II criteria, the required frequency of abdominal pain is at least once a week for a period of 12 weeks during the previous 12 months. The reason for the higher requirement of pain in the Questionnaire is possibly to concentrate a more homogenous IBS group for research purposes and clinical trials, although this has not been commented on by the authors of the Rome II book[19]. In the widely used Rome II Modular Questionnaire, the required frequency of abdominal pain or discomfort is also “often”, meaning in the last three months “the symptoms were present during at least three

weeks (at least one day in each week)"[19]. This interpretation of "often" would generate an IBS prevalence of 9.3% in our population sample. In the Rome III Questionnaire, the required frequency of abdominal pain or discomfort is at least two to three days a month. In pathophysiology research and clinical trials, however, a frequency of at least two days a week during screening evaluation is recommended for subject eligibility[276].

Rome II criteria have been criticised as too restrictive for research and practice[75]. In addition, poor agreement between IBS diagnosis by general practitioners and Rome II criteria has been shown[277]. A clinician's diagnosis is usually based on a global conception of a patient's symptoms and clinical signs rather than on a standardised questionnaire. According to the Rome II definition, a high proportion of patients with IBS-type symptoms, but only occasional abdominal pain or discomfort, would fit into categories with no requirement of pain, such as functional constipation, functional diarrhoea, or unspecified functional bowel disorder[278].

## Depression and anxiety

The presence of depressive symptoms and anxiety is higher in the IBS population than among controls regardless of applied criteria. Half of the respondents fulfilling the Rome II criteria reported depressive symptoms or anxiety (II). Of those with at least one physician visit for GI symptoms, 43% had depressive symptoms, but these symptoms were not independent predictors of GI visits. Our results show that psychiatric comorbidity in IBS is not limited to healthcare seekers, but also exists among non-consulters (II). In two studies from Scandinavia, high frequencies of psychiatric distress and mood disorders were detected among both IBS consulters and non-consulters, supporting our findings[42,135].

Depressive symptoms are prevalent in the general population regardless of IBS. In our study, 17% of participants reported at least mild depressive symptoms. Prevalence of clinical depression in Finnish population studies have ranged between 5% to 9%[138,279]. Differences between prevalence estimates are probably due to different study methodology as these studies used the University of Michigan Composite International Diagnostic Interview (UM-CICI). Moreover, we used a cut-off level of 4/5 in R-BDI-SF, originally suggested for general population screening[267], while a higher cut-off point of 7/8 has also been recommended to increase the specificity of R-BDI-SF for detection of depression among adolescents[280]. Thus, our results also include mild depressive symptoms.

Depressive symptoms were associated with a high rate of GI symptoms, and IBS was more than three times as common among subject with depressiveness. In addition, presence of depressive symptoms was associated with increased use of healthcare services and work absenteeism for GI reasons (III).

In former studies, high co-occurrence of psychiatric and GI symptoms has been observed among healthcare users with IBS[281-283]. Our results suggest that overlap of depression and GI symptoms is also considerable in general population. Possible reasons for such overlap include common pathophysiological mechanisms regulating both mood

and brain-gut interactions[284,285], or a lower threshold of interpreting signals from GI tract as disturbing. No conclusions on causality, however, can be made from the present cross-sectional study.

## Comorbidity

In the general population, several somatic and psychiatric symptoms are overrepresented among subjects fulfilling Rome II criteria of IBS.

Almost half of the subjects meeting Rome II IBS criteria reported symptoms consistent with dyspepsia, compared with only 6% of those without IBS. Earlier reports show a similar overlap with IBS and functional dyspepsia[9,152,286]. This high co-occurrence is suggestive of a common pathophysiological basis, or only one disorder with different symptom manifestations.

Of those meeting the Rome II IBS criteria, 69% reported somatic symptoms, such as headache, back pain, allergy, or asthma compared to 35% among controls. In previous studies, chronic headache are reported by 23 to 35% and back pain by 28 to 81% of subjects with IBS[287,288], in line with our findings.

Some studies report an increased rate of asthma or bronchial hyper-responsiveness among subjects with IBS[92,161,289]. In the present study, diagnosis of asthma was reported 2.4 times more frequently by subjects with IBS than by controls (II). IBS has also been associated with a positive methacholine test[290], although not confirmed[291,292]. Several theories of a common pathogenesis exist to explain the co-occurrence of asthma and IBS. A disorder affecting both bronchial and GI tract involved with smooth muscle, neuromuscular, or inflammatory system is possible, but needs further study. No significant difference was detected, however, in the frequency of food allergy in our study (II).

## Healthcare seeking

IBS is associated with an elevated rate of physician visits for both GI and non-GI reasons. In our study, 48 to 49% of subjects meeting either Rome criteria had consulted a physician for abdominal symptoms during the previous year (I), in line with consultation rates in former studies[229,231]. In a previous study from Finland, 75 to 81% of the population had made at least one physician visit for any reason during the previous year[293]. In our study, 80% of subjects in the control group had at least one non-GI visit, compared with an even higher share of 86 to 89% of those meeting any IBS criteria. The higher share of non-GI consultations in IBS is likely due to the high rates of non-GI comorbidity association.

### Predictors of GI consultations

The main predictors for GI visits were disturbing abdominal symptoms, severe abdominal pain, dyspeptic symptoms, lactose intolerance, and IBS (II). Of the non-GI symptoms, only insomnia and headache, but not depression nor anxiety, were predictive for GI visits. This is in line with an Australian study by Talley *et al.*[229], where pain severity, but not psychological comorbidity, was an independent predictor of GI visits.

In previous literature, the role of psychiatric symptoms as predictors of healthcare use is inconclusive. Anxiety, depression, somatisation, and lowered QoL are associated with increased healthcare use[108,231,234,294]. In other population based studies, however, psychological factors did not explain healthcare seeking for abdominal reasons[229,231].

In our study, co-occurrence of IBS and other somatic or psychiatric symptoms did not elevate the likelihood of consulting for GI reasons. In fact, the combination of lactose intolerance and IBS lowered the probability of consultation, perhaps because of such individuals having already consulted earlier and attributing their GI symptoms as lactose ingestion not needing physician care. Overall, our results indicate that the predictors for consulting are not different for those with IBS compared to controls.

### Predictors of non-GI consultations

Presence of IBS had no impact on consultation rates for non-GI visits. Young age and presence of a chronic medical condition were the strongest predictors for them. The need for physician consultations and statements for applying for a job, studying, or driver's license may explain young age as a predictor for non-GI visits. Of the GI disorders and symptoms listed (dyspepsia, IBS, diarrhoea, constipation, lactose intolerance, history of abdominal surgery, celiac disease, and abdominal pain), only the presence of dyspeptic symptoms predicted non-GI visits. One reason for dyspeptic symptoms predicting non-GI visits may be the patient's concern of possible serious disease, such as heart disease causing the upper abdominal symptoms[295]. It is also possible that dyspepsia is associated with other non-GI comorbidities, but not covered by our questionnaire, influencing healthcare use.

## Societal costs

Due to high prevalence rates and frequent healthcare use, IBS generates a considerable economic burden. Our study indicates that 2 to 5% of the working age population annually consults a physician for their IBS symptoms. Those meeting Rome II criteria incur 1.7 times higher GI related costs per subject as those meeting the more lax Manning 2 criteria (497€ vs. 295€) (IV). Nationwide, however, expenditures are almost twice as high for Manning 2 as Rome II criteria (154M€ vs. 82M€), because of the considerable difference in the prevalence estimates by the criteria: 15.9% by Manning and 5.1% by Rome II

criteria. Overall, we obtained more modest individual GI costs compared to previous studies assessing IBS costs in Europe[245,246].

No gender difference was detected in GI related costs per subject, although some studies have found up to 3.3 times higher consultation rates for females[105,116,233,296]. In the study by Drossman *et al.*[105], 44% of females and 35% of males with a functional GI disorder by Rome I criteria had visited a physician for GI symptoms during the previous year. In our study, 53% of females and 44% of males fulfilling Rome I criteria for IBS had made at least one physician visit for GI reasons ($p = 0.205$). In the database study by Shih *et al.*[233], differences in healthcare use between genders were partly explained by gender differences in the population prevalence of IBS. Other studies from the UK, US, and Australia have, however, found no difference in consultation behaviour between genders[77,229,231]. Likewise, two previous studies reported no gender difference in IBS costs[243,246]. It is possible that cultural differences in healthcare use between genders in different countries exist, but this issue needs further study.

The principal cost component was the share of physician visits, covering 40 to 42% of the total annual costs. The average annual number of visits for GI symptoms ranged between 1.0 (Manning 2 criteria) and 1.8 (Rome II criteria). Higher number of annual physician visits for GI reasons have been reported by France (7.8)[246], Spain (2.9)[247], the UK (3.9)[249], and the US (3.7)[249]. In the US Householder study[105], the number of GI visits was 1.64, closer to our findings.

Of the total GI expenditures, indirect costs covered 32 to 34% (IV). In previous studies, a wide range of 16 to 82% has been reported to represent the share of indirect costs in IBS. In a review, three out of five studies reported a proportion of more than 70% of the total costs. The main factor of indirect costs is sick leave cost. In our study, the mean number of sick leave days was 0.9 for those meeting Manning 2 criteria, considerably less than the 2.2 days in the French study[246]. Previous studies from the UK and US have reported even higher numbers of IBS-related sick leave days, ranging between 8.5 and 21.6 per year[248]. In our study, almost one third of subjects meeting Rome II criteria reported impaired performance at work weekly or more often indicating that they tend to go to work despite of GI symptoms rather than take sick leave. This may partly explain the lower than previously detected missed work days in our present study.

The duration of GI symptoms had no effect on total GI costs, or costs of endoscopies. IBS is a chronic disorder typically with fluctuating severity of symptoms. Repeating diagnostic procedures is not suggested, as the diagnosis is not likely to change over time[81,297]. That the costs of endoscopies were not lower for those with several years of IBS symptoms may indicate that contrary to guideline recommendations, diagnostic procedures are repeated, or the first procedure is performed late in the course of GI symptoms. On the other hand, situations not covered by a cross sectional setting, such as a change in symptoms or appearance of new alarm symptoms, may also explain the finding.

In our present study, subjects meeting Manning 2 or Rome II criteria made 1.3 to 1.4 times more non-GI physician visits than controls. The direct costs of GI symptoms and non-GI visits amounted to 98M€ by Rome II and 230M€ by Manning 2 criteria, equivalent to a substantial share of 2 to 5% of the 4 562M€ expenditures on outpatient healthcare and medicines in Finland (IV). Besides direct and indirect costs, IBS incurs intangible costs

related to suffering from pain and reduced QoL, which cannot be properly measured in monetary terms. An integral approach to IBS by physicians, to also consider comorbid conditions, may produce a more favourable course in IBS patients and even reduce healthcare expenditures.

# SUMMARY AND CONCLUSIONS

Our study investigated the prevalence of IBS according to varying diagnostic criteria, somatic and psychiatric comorbity, healthcare resource use, and societal costs.

The prevalence of IBS shows a substantial variation depending on the criteria applied. Manning criteria with at least two of the six Manning symptoms represent the broadest interpretation of IBS giving a three-fold prevalence figure compared to Rome II, the strictest criteria. Subjects fulfilling Rome II criteria form a subgroup of those fulfilling Manning 2 criteria with more severe GI symptoms, more frequent health care resource use and higher societal costs per subject.

IBS, by Rome II criteria, is associated with a high level of somatic and psychiatric comorbidity among both healthcare consulters and non-consulters. Healthcare seeking for GI symptoms is predicted by symptom severity rather than psychiatric comorbidity. Presence of dyspeptic symptoms also predicts healthcare seeking for non-GI symptoms.

Depressive symptoms are prevalent in the general population and are associated with an increased level of GI symptoms, physician visits, and work absenteeism for GI symptoms.

The economic burden of IBS is considerable. Direct costs of GI symptoms and non-GI consultations correspond to a share of up to 5% of the outpatient healthcare and medicine expenditures in Finland.

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**1. Vastaajan sukupuoli**
☐ Nainen ☐ Mies

**2. Vastaajan ikä:** ☐☐ vuotta

**3. Siviilisääty**
☐ Naimaton
☐ Naimisissa
☐ Avoliitossa
☐ Leski
☐ Eronnut tai asumuserossa

**4. Mikä on peruskoulutuksenne?**
☐ Kansakoulu tai vähemmän
☐ Keskikoulu tai peruskoulu
☐ Osa lukiota
☐ Ylioppilas

**5. Minkälaista työaikaa noudatatte?**
☐ Säännöllinen päivätyö
☐ 2-vuorotyö
☐ 3-vuorotyö
☐ Yötyö
☐ Muu epäsäännöllinen työaika
☐ En ole töissä

**6. Onko terveydentilanne yleisesti ottaen**
☐ Erinomainen
☐ Varsin hyvä
☐ Hyvä
☐ Tyydyttävä
☐ Huono

**7. Onko lääkäri todennut Teillä maitosokerin imeytymishäiriön eli laktoosi-intoleranssin?**
☐ Ei ☐ Kyllä ☐ En osaa sanoa

**8. Onko lääkäri todennut Teillä keliakia-sairauden?**
☐ Ei ☐ Kyllä ☐ En osaa sanoa

**9. Onko lääkäri todennut Teillä lapsuudessa (alle 15 -vuotiaana) seuraavia sairauksia:**

**a) Ruoka-aineallergia?**
☐ Ei ☐ Kyllä ☐ En osaa sanoa

**b) Atooppinen ihottuma?**
☐ Ei ☐ Kyllä ☐ En osaa sanoa

**c) Astma?**
☐ Ei ☐ Kyllä ☐ En osaa sanoa

**d) Allerginen nuha?**
☐ Ei ☐ Kyllä ☐ En osaa sanoa

**10. Esiintyikö Teillä lapsuudessa (alle 15 -vuotiaana) muita enemmän vatsakipuja?**
☐ Ei ☐ Kyllä ☐ En osaa sanoa

**11. Onko umpilisäkkeenne leikattu?**
☐ Ei ☐ Kyllä, milloin? Vuonna ☐☐☐☐

**12. Onko Teille tehty sappileikkaus?**
☐ Ei ☐ Kyllä, milloin? Vuonna ☐☐☐☐

**13. Onko Teille tehty jokin muu suoliston tai vatsan alueen leikkaus?**
☐ Ei ☐ Kyllä, milloin? Vuonna ☐☐☐☐

**Mikä leikkaus?**

_____

_____

_____

**14. Onko Teille tehty seuraavia mahasuolikanavan tutkimuksia:**

**a) Mahalaukun tähystys?**
☐ Ei ☐ Kyllä, viimeksi vuonna ☐☐☐☐

**b) Paksusuolen tähystys?**
☐ Ei ☐ Kyllä, viimeksi vuonna ☐☐☐☐

**15. Onko Teillä jokin pitkäaikaissairaus?**
☐ Ei ☐ Kyllä, mikä?

_____

_____

**16. Onko Teillä säännöllinen lääkitys?**
☐ Ei ☐ Kyllä, mikä?

Listatkaa tähän kaikki säännöllisesti käyttämänne lääkkeet, myös käsikauppalääkkeet:

_____

_____

_____

**17. Kuinka usein Teillä on ollut vatsakipua tai vatsavaivaa (vatsan seudun epämiellyttävää tunnetta) viimeksi kuluneen vuoden aikana?**

☐ Harvoin tai ei ollenkaan
☐ Toisinaan (useammin kuin yhtenä päivänä kymmenestä)
☐ Usein (useammin kuin yhtenä päivänä neljästä)
☐ Hyvin usein (vähintään joka toinen päivä)
☐ Jatkuvasti (päivittäin)

**Mikäli vastasitte "harvoin tai ei ollenkaan", voitte siirtyä suoraan kysymykseen 30, muussa tapauksessa vastatkaa vielä seuraaviin kysymyksiin:**

**18. Kuinka usein viimeksi kuluneen vuoden aikana vatsakipu tai vatsavaiva häiritsi päivittäisiä askareitanne?**

☐ Harvoin tai ei ollenkaan
☐ Toisinaan (useammin kuin yhtenä päivänä kymmenestä)
☐ Usein (useammin kuin yhtenä päivänä neljästä)
☐ Hyvin usein (vähintään joka toinen päivä)
☐ Jatkuvasti (päivittäin)

**19. Kuinka voimakasta edellä mainittu vatsaoire on yleensä ollut viimeisen vuoden aikana?**

☐ Lievää (voi helposti jäädä huomaamatta, ellei sitä ajattele)
☐ Kohtalaista (oire on olemassa, mutta ei häiritse päivän toimintoja)
☐ Voimakasta (oire häiritsee päivän toimintoja)
☐ Erittäin voimakasta (oire häiritsee merkittävästi päivän toimintoja)

**20. Helpottuiko edellä mainittu vatsakipu tai vatsavaiva ulostamisen jälkeen?**

☐ Harvoin tai ei ollenkaan
☐ Toisinaan (useammin kuin yhtenä kertana kymmenestä)
☐ Usein (useammin kuin yhtenä kertana neljästä)
☐ Hyvin usein (vähintään joka toinen kerta)
☐ Lähes aina

**21. Muuttuiko suolentoimintanne (ulostamistiheys) tavallista tiheämmäksi edellä mainitun vatsakivun tai -vaivan alkaessa?**

☐ Harvoin tai ei ollenkaan
☐ Toisinaan (useammin kuin yhtenä kertana kymmenestä)
☐ Usein (useammin kuin yhtenä kertana neljästä)
☐ Hyvin usein (vähintään joka toinen kerta)
☐ Lähes aina

**22. Muuttuiko suolentoimintanne tavallista harvemmaksi edellä mainitun vatsakivun tai -vaivan alkaessa?**

☐ Harvoin tai ei ollenkaan
☐ Toisinaan (useammin kuin yhtenä kertana kymmenestä)
☐ Usein (useammin kuin yhtenä kertana neljästä)
☐ Hyvin usein (vähintään joka toinen kerta)
☐ Lähes aina

**23. Muuttuiko ulosteenne koostumus tavallista löysemmäksi edellä mainitun vatsakivun tai -vaivan alkaessa?**

☐ Harvoin tai ei ollenkaan
☐ Toisinaan (useammin kuin yhtenä kertana kymmenestä)
☐ Usein (useammin kuin yhtenä kertana neljästä)
☐ Hyvin usein (vähintään joka toinen kerta)
☐ Lähes aina

**24. Muuttuiko ulosteenne koostumus tavallista kovemmaksi edellä mainitun vatsakivun tai -vaivan alkaessa?**

☐ Harvoin tai ei ollenkaan
☐ Toisinaan (useammin kuin yhtenä kertana kymmenestä)
☐ Usein (useammin kuin yhtenä kertana neljästä)
☐ Hyvin usein (vähintään joka toinen kerta)
☐ Lähes aina

**25. Mitkä tekijät pahentavat vatsaoireitanne?**

**a) Ruokailu?**

☐ Ei pahenna ☐ Pahentaa joskus oireita ☐ Pahentaa usein oireita
☐ Pahentaa aina oireita ☐ En osaa sanoa

**b) Maito tai maitotuotteet?**

☐ Eivät pahenna ☐ Pahentavat joskus oireita ☐ Pahentavat usein oireita
☐ Pahentavat aina oireita ☐ En osaa sanoa

**Mitä oireita saatte maitotuotteista?** _____

**Mitkä maitotuotteet aiheuttavat oireita?** _____

**c) Viljatuotteet?**

☐ Eivät pahenna ☐ Pahentavat joskus oireita ☐ Pahentavat usein oireita
☐ Pahentavat aina oireita ☐ En osaa sanoa

**Mitä oireita saatte viljatuotteista?** _____

**Mitkä viljatuotteet aiheuttavat oireita?** _____

**d) Jotkin muut tekijät tai ruoka-aineet? Mitkä?** _____

_____

**Minkälaisia oireita ne aiheuttavat?** _____

_____

**26. Onko Teillä ollut viimeksi kuluneen vuoden aikana <u>usein</u> vatsakipua tai vatsavaivaa (vatsan seudun epämiellyttävää tunnetta)? <u>Usein</u> tarkoittaa tässä yhteydessä oireen esiintymistä vähintään kerran viikossa ainakin 12 eri viikkona viimeisen vuoden aikana.**

☐ Ei ☐ Kyllä

**27. Kuinka usein viimeksi kuluneen vuoden aikana Teillä on ollut <u>ylävatsalla</u> (navan yläpuolella) tuntuvaa kipua? Närästystä eli rintalastan takana tuntuvaa polttelua ei lasketa mukaan.**

☐ Harvoin tai ei ollenkaan
☐ Toisinaan (useammin kuin yhtenä päivänä kymmenestä)
☐ Usein (useammin kuin yhtenä päivänä neljästä)
☐ Hyvin usein (vähintään joka toinen päivä)
☐ Jatkuvasti tai lähes jatkuvasti

**28. Kuinka usein viimeisen vuoden aikana Teillä on ollut <u>ylävatsalla</u> tuntuvaa muuta epämukavuuden tunnetta, esim. pahoinvointia, ylävatsan turvotusta tai ruokailun yhteydessä varhaista vatsan täyttymisen tunnetta?**

☐ Harvoin tai ei ollenkaan
☐ Toisinaan (useammin kuin yhtenä päivänä kymmenestä)
☐ Usein (useammin kuin yhtenä päivänä neljästä)
☐ Hyvin usein (vähintään joka toinen päivä)
☐ Jatkuvasti tai lähes jatkuvasti

**Jos vastasitte "harvoin tai ei ollenkaan", voitte siirtyä kysymykseen 30, muussa tapauksessa vastatkaa vielä seuraavaan:**

**29. Kuinka voimakasta edellä mainittu <u>ylävatsaoire</u> on yleensä ollut viimeisen vuoden aikana?**

☐ Lievää (voi helposti jäädä huomaamatta, ellei sitä ajattele)
☐ Kohtalaista (oire on olemassa, mutta ei häiritse päivän toimintoja)
☐ Voimakasta (oire häiritsee päivän toimintoja)
☐ Erittäin voimakasta (oire häiritsee merkittävästi päivän toimintoja)

**30. Kuinka usein viimeksi kuluneen vuoden aikana Teillä oli enemmän kuin kolme ulostuskertaa päivässä?**
☐ Harvoin tai ei ollenkaan
☐ Toisinaan (useammin kuin yhtenä päivänä kymmenestä)
☐ Usein (useammin kuin yhtenä päivänä neljästä)
☐ Hyvin usein (vähintään joka toinen päivä)
☐ Jatkuvasti tai lähes jatkuvasti

**31. Kuinka usein viimeksi kuluneen vuoden aikana Teillä oli vähemmän kuin kolme ulostuskertaa viikossa?**
☐ Harvoin tai ei ollenkaan
☐ Toisinaan (useammin kuin yhtenä viikkona kymmenestä)
☐ Usein (useammin kuin yhtenä viikkona neljästä)
☐ Hyvin usein (vähintään joka toinen viikko)
☐ Jatkuvasti tai lähes jatkuvasti

**32. Kuinka usein viimeksi kuluneen vuoden aikana ulosteenne oli kovaa, kokkaremaista tai papanamaista?**
☐ Harvoin tai ei ollenkaan
☐ Toisinaan (useammin kuin yhtenä kertana kymmenestä)
☐ Usein (useammin kuin yhtenä kertana neljästä)
☐ Hyvin usein (vähintään joka toinen kerta)
☐ Jatkuvasti tai lähes jatkuvasti

**33. Kuinka usein viimeksi kuluneen vuoden aikana ulosteenne oli löysää tai vetistä?**
☐ Harvoin tai ei ollenkaan
☐ Toisinaan (useammin kuin yhtenä kertana kymmenestä)
☐ Usein (useammin kuin yhtenä kertana neljästä)
☐ Hyvin usein (vähintään joka toinen kerta)
☐ Jatkuvasti tai lähes jatkuvasti

**34. Kuinka usein viimeksi kuluneen vuoden aikana Teille jäi ulostamistapahtuman jälkeen tunne, että peräsuolenne ei tyhjentynyt kunnolla?**
☐ Harvoin tai ei ollenkaan
☐ Toisinaan (useammin kuin yhtenä kertana kymmenestä)
☐ Usein (useammin kuin yhtenä kertana neljästä)
☐ Hyvin usein (vähintään joka toinen kerta)
☐ Jatkuvasti tai lähes jatkuvasti

**35. Kuinka usein viimeksi kuluneen vuoden aikana Teidän oli ponnisteltava runsaasti saadaksenne peräsuolenne tyhjentymään?**
☐ Harvoin tai ei ollenkaan
☐ Toisinaan (useammin kuin yhtenä kertana kymmenestä)
☐ Usein (useammin kuin yhtenä kertana neljästä)
☐ Hyvin usein (vähintään joka toinen kerta)
☐ Aina tai lähes aina

**36. Kuinka usein viimeksi kuluneen vuoden aikana Teillä on ollut pakottava ulostamisen tarve, jonka vuoksi Teidän on täytynyt kiirehtiä wc:hen?**
☐ Harvoin tai ei ollenkaan
☐ Toisinaan (useammin kuin yhtenä kertana kymmenestä)
☐ Usein (useammin kuin yhtenä kertana neljästä)
☐ Hyvin usein (vähintään joka toinen kerta)
☐ Aina tai lähes aina

**37. Kuinka usein viimeksi kuluneen vuoden aikana olette huomannut limaa ulosteissanne?**
☐ Harvoin tai ei ollenkaan
☐ Toisinaan (useammin kuin yhtenä kertana kymmenestä)
☐ Usein (useammin kuin yhtenä kertana neljästä)
☐ Hyvin usein (vähintään joka toinen kerta)
☐ Aina tai lähes aina

**38. Kuinka usein viimeksi kuluneen vuoden aikana Teillä on ollut vatsan turvotusta?**
☐ Harvoin tai ei ollenkaan
☐ Toisinaan (useammin kuin yhtenä päivänä kymmenestä)
☐ Usein (useammin kuin yhtenä päivänä neljästä)
☐ Hyvin usein (vähintään joka toinen päivä)
☐ Jatkuvasti tai lähes jatkuvasti

**39. Kuinka monta kertaa viimeisen vuoden aikana olette käynyt lääkärissä vatsavaivojen vuoksi?**
☐ En kertaakaan
☐ 1-2 kertaa
☐ 3-5 kertaa
☐ 6-10 kertaa
☐ Yli 10 kertaa

**40. Kuinka monta kertaa viimeisen vuoden aikana olette käynyt lääkärin vastaanotolla muiden syiden kuin vatsavaivojen vuoksi?**
☐ En kertaakaan
☐ 1-2 kertaa
☐ 3-5 kertaa
☐ 6-10 kertaa
☐ Yli 10 kertaa

**41. Kuinka monta päivää olette ollut vatsavaivojen takia poissa töistä viimeisen vuoden aikana?**
☐ 0 päivää
☐ 1-3 päivää
☐ 4-6 päivää
☐ 7-20 päivää
☐ Yli 20 päivää
☐ En ole ollut työssä viimeisen vuoden aikana

**42. Kuinka usein olette viimeisen vuoden aikana käyttänyt vatsaoireiden vuoksi lääkärin määräämiä lääkkeitä?**
☐ En lainkaan
☐ Harvemmin kuin kerran kuukaudessa
☐ Keskimäärin 1-3 kertaa kuukaudessa
☐ Keskimäärin 1-3 kertaa viikossa
☐ Päivittäin tai lähes päivittäin

**43. Kuinka usein olette viimeisen vuoden aikana käyttänyt vatsaoireiden vuoksi reseptivapaita käsikauppalääkkeitä?**
☐ En lainkaan
☐ Harvemmin kuin kerran kuukaudessa
☐ Keskimäärin 1-3 kertaa kuukaudessa
☐ Keskimäärin 1-3 kertaa viikossa
☐ Päivittäin tai lähes päivittäin

**44. Kuinka usein Teillä esiintyy seuraavia oireita?**

**a) Päänsärkyä?**
☐ Harvemmin kuin kerran kuukaudessa
☐ 1-3 kertaa kuukaudessa
☐ 1-3 kertaa viikossa
☐ Useammin kuin 3:sti viikossa

**b) Selkäkipua?**
☐ Harvemmin kuin kerran kuukaudessa
☐ 1-3 kertaa kuukaudessa
☐ 1-3 kertaa viikossa
☐ Useammin kuin 3:sti viikossa

Lopuksi esitämme eräitä kysymyksiä, jotka käsittelevät mielialan erilaisia piirteitä. Vastatkaa kuhunkin kysymykseen merkitsemällä rasti siihen kysymyksen jäljessä olevaan ruutuun, joka parhaiten kuvaa Teidän tilannettanne tällä hetkellä. Valitkaa kustakin kysymyksestä vain yksi vaihtoehto älkääkä jättäkö yhtään kysymystä väliin.

**45. Minkälainen Teidän mielialanne on?**
☐ Mielialani on melko valoisa ja hyvä
☐ En ole alakuloinen tai surullinen
☐ Tunnen itseni alakuloiseksi tai surulliseksi
☐ Olen alakuloinen jatkuvasti enkä pääse siitä
☐ Olen niin masentunut ja alavireinen, etten kestä enää

**46. Miten suhtaudutte tulevaisuuteen?**
☐ Suhtaudun tulevaisuuteeni toiveikkaasti
☐ En suhtaudu tulevaisuuteeni toivottomasti
☐ Tulevaisuus tuntuu minusta melko masentavalta
☐ Minusta tuntuu, ettei minulla ole tulevaisuudelta mitään odotettavaa
☐ Tulevaisuus tuntuu minusta toivottomalta, enkä jaksa uskoa, että asiat muuttuisivat parempaan päin

**47. Miten katsotte elämänne sujuneen?**
☐ Olen elämässäni onnistunut huomattavan usein
☐ En tunne epäonnistuneeni elämässäni
☐ Minusta tuntuu, että olen epäonnistunut pyrkimyksissäni tavallista useammin
☐ Elämäni on tähän saakka ollut vain sarja epäonnistumisia
☐ Tunnen epäonnistuneeni täydellisesti ihmisenä

**48. Miten tyytyväiseksi tai tyytymättömäksi tunnette itsenne?**
☐ Olen varsin tyytyväinen elämääni
☐ En ole erityisen tyytymätön
☐ En nauti asioista samalla tavalla kuin ennen
☐ Minusta tuntuu, etten saa tyydytystä juuri mistään
☐ Olen täysin tyytymätön kaikkeen

**49. Minkälaisena pidätte itseänne?**
☐ Tunnen itseni melko hyväksi
☐ En tunne itseäni huonoksi ja arvottomaksi
☐ Tunnen itseni huonoksi ja arvottomaksi melko usein
☐ Nykyään tunnen itseni arvottomaksi melkein aina
☐ Olen kerta kaikkiaan arvoton ja huono

**50. Onko Teillä pettymyksen tunteita?**
☐ Olen tyytyväinen itseeni ja suorituksiini
☐ En ole pettynyt itseni suhteen
☐ Olen pettynyt itseni suhteen
☐ Minua inhottaa oma itseni
☐ Vihaan itseäni

**51. Onko Teillä itsenne vahingoittamiseen liittyviä ajatuksia?**
☐ Minulla ei ole koskaan ollut itsemurha-ajatuksia
☐ En ajattele enkä halua vahingoittaa itseäni
☐ Minusta tuntuu, että olisi parempi, jos olisin kuollut
☐ Minulla on tarkat suunnitelmat itsemurhasta
☐ Tekisin itsemurhan, jos siihen olisi mahdollisuus

**52. Miten suhtaudutte vieraitten ihmisten tapaamiseen?**
☐ Pidän ihmisten tapaamisesta ja juttelemisesta
☐ En ole menettänyt kiinnostustani muihin ihmisiin
☐ Toiset ihmiset eivät enää kiinnosta minua niin paljon kuin ennen
☐ Olen melkein kokonaan menettänyt mielenkiintoni ja tunteeni toisia ihmisiä kohtaan
☐ Olen menettänyt mielenkiintoni muihin ihmisiin, enkä välitä heistä lainkaan

**53. Miten koette päätösten tekemisen?**
☐ Erilaisten päätösten tekeminen on minulle helppoa
☐ Pystyn tekemään päätöksiä samoin kuin ennenkin
☐ Varmuuteni on vähentynyt ja yritän lykätä päätösten tekoa
☐ Minulla on suuria vaikeuksia päätösten teossa
☐ En pysty enää lainkaan tekemään ratkaisuja ja päätöksiä

**54. Minkälaisena pidätte olemustanne ja ulkonäköänne?**
☐ Olen melko tyytyväinen ulkonäköön ja olemukseeni
☐ Ulkonäössäni ei ole minua haittaavia piirteitä
☐ Olen huolissani siitä, että näytän epämiellyttävältä
☐ Minusta tuntuu, että näytän rumalta
☐ Olen varma, että näytän rumalta ja vastenmieliseltä

**55. Minkälaista Teidän nukkumisenne on?**
☐ Minulla ei ole nukkumisessa minkäänlaisia vaikeuksia
☐ Nukun yhtä hyvin kuin ennenkin
☐ Herätessäni aamuisin olen paljon väsyneempi kuin ennen
☐ Minua haittaa unettomuus
☐ Kärsin unettomuudesta, nukahtamisvaikeuksista tai liian aikaisin kesken unien heräämisistä

**56. Tunnetteko väsymystä tai uupumusta?**
☐ Väsyminen on minulle lähes täysin vierasta
☐ En väsy helpommin kuin tavallisestikaan
☐ Väsyn nopeammin kuin ennen
☐ Vähäinenkin työ väsyttää ja uuvuttaa minua
☐ Olen liian väsynyt tehdäkseni mitään

**57. Minkälainen ruokahalunne on?**
☐ Ruokahalussani ei ole mitään hankaluuksia
☐ Ruokahaluni on ennallaan
☐ Ruokahaluni on huonompi kuin ennen
☐ Ruokahaluni on nyt paljon huonompi kuin ennen
☐ Minulla ei ole enää lainkaan ruokahalua

**58. Oletteko ahdistunut tai jännittynyt?**
☐ Pidän itseäni melko hyvähermoisena enkä ahdistu kovinkaan helposti
☐ En tunne itseäni ahdistuneeksi tai "huonohermoiseksi"
☐ Ahdistun ja jännityn melko helposti
☐ Tulen erityisen helposti tuskaiseksi, ahdistuneeksi tai jännittyneeksi
☐ Tunnen itseni jatkuvasti ahdistuneeksi ja tuskaiseksi kuin hermoni olisivat "loppuun kuluneet"

**Tarkistakaa vielä, että olette vastannut kaikkiin kysymyksiin ja palauttakaa kaavake oheisessa palautuskuoressa. KIITOS VAIVANNÄÖSTÄNNE!**

**1. Kuinka kauan Teillä on ollut vatsavaivoja?**

☐ Alle vuoden ajan ☐ 1-3 vuotta ☐ 3-10 vuotta ☐ Yli 10 vuotta

**2. Ovatko vatsaoireenne viimeisen 3 kuukauden aikana pysyneet ennallaan, lisääntyneet vai vähentyneet?**

☐ Pysyneet ennallaan ☐ Lisääntyneet ☐ Vähentyneet

**3. Luettelemme seuraavaksi 5 erilaista vatsaoiretta. Nimetkää näistä pahin oireenne laittamalla numero 1 oireen vieressä olevaan ruutuun, toiseksi pahin numerolla 2 jne. Mikäli kärsitte jostakin muusta vatsaoireesta, kirjoittakaa se vapaaseen tilaan ja merkitkää sen viereen sopivaksi katsomanne numero oireen hankaluuden mukaan.**

Vatsakipu ..... ☐

Vatsan turvotus..... ☐

Ilmavaivat..... ☐

Ripuli..... ☐

Ummetus..... ☐

Jokin muu oire, mikä?_____ ☐

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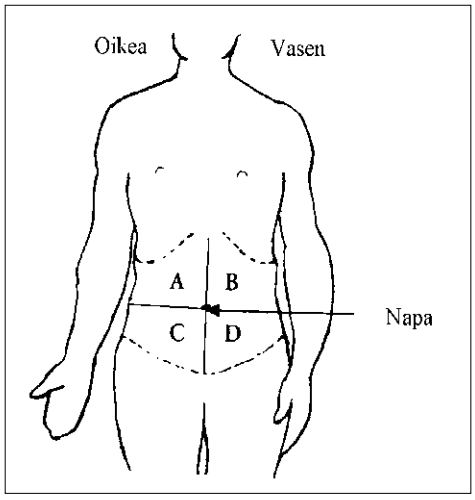
**4. Kuinka usein Teillä on ollut vatsakipua tai vatsavaivaa (vatsan seudun epämiellyttävää tunnetta) <u>viimeksi kuluneen 3 kuukauden aikana</u>?**

☐ Harvoin tai ei ollenkaan
☐ Toisinaan (useammin kuin yhtenä päivänä kymmenestä)
☐ Usein (useammin kuin yhtenä päivänä neljästä)
☐ Hyvin usein (vähintään joka toinen päivä)
☐ Jatkuvasti (päivittäin)

**Mikäli vastasitte "harvoin tai ei ollenkaan", voitte siirtyä seuraavalle sivulle kysymykseen 7, muussa tapauksessa vastatkaa vielä seuraaviin kysymyksiin:**

**5. Millä alueella vatsakipunne tai -vaivanne tuntuu? Valitkaa oheisen kaavakuvan mukaisesti tilannettanne parhaiten kuvaava alue A,B,C tai D. Voitte valita myös useamman kuin yhden kirjaimen, mikäli oireenne tuntuu laajemmalla alueella. Merkitkää vastauksenne rastilla (X) asianomaisten kirjainten kohdalla oleviin ruutuihin.**

☐ A
☐ B
☐ C
☐ D




**6. Mikäli valitsitte edelliseen kysymykseen useamman kuin yhden alueen, pyydämme Teitä vielä arvioimaan, millä näistä alueista oleva kipu tai vaiva häiritsee Teitä eniten? Valitkaa nyt vain yksi alue yllä olevasta kaavakuvasta.**

☐ A
☐ B
☐ C
☐ D
☐ En osaa sanoa

**7. Kuinka monta kertaa Teille on tehty vatsavaivojenne vuoksi seuraavia tutkimuksia?**

**Paksusuolen tähystys?**
☐ Ei kertaakaan ☐ Kerran ☐ 2 kertaa ☐ 3 kertaa ☐ Yli 3 kertaa

**Paksusuolen röngtenkuvaus?**
☐ Ei kertaakaan ☐ Kerran ☐ 2 kertaa ☐ 3 kertaa ☐ Yli 3 kertaa

**Mahalaukun tähystys?**
☐ Ei kertaakaan ☐ Kerran ☐ 2 kertaa ☐ 3 kertaa ☐ Yli 3 kertaa

**Vatsan alueen ultraäänitutkimus?**
☐ Ei kertaakaan ☐ Kerran ☐ 2 kertaa ☐ 3 kertaa ☐ Yli 3 kertaa

**8. Oletteko käynyt lääkärissä vatsavaivojenne takia viimeisen vuoden aikana?**

☐ Kyllä ☐ En

**Mikäli vastasitte "En", voitte siirtyä seuraavalle sivulle kysymykseen 14, mikäli vastasitte "Kyllä", jatkakaa seuraavasta kysymyksestä:**

**9. Kuinka monta kertaa viimeisen vuoden aikana olette käynyt vatsavaivojenne takia terveyskeskuslääkärin vastaanotolla?**

☐ En kertaakaan ☐ Kerran ☐ 2 kertaa ☐ 3 kertaa ☐ 4-6 kertaa ☐ yli 6 kertaa

**10. Kuinka monta kertaa viimeisen vuoden aikana olette käynyt vatsavaivojenne takia työterveyslääkärin vastaanotolla?**

☐ En kertaakaan ☐ Kerran ☐ 2 kertaa ☐ 3 kertaa ☐ 4-6 kertaa ☐ yli 6 kertaa

**11. Kuinka monta kertaa viimeisen vuoden aikana olette käynyt vatsavaivojenne takia sairaalan ajanvarauspoliklinikalla (sisätautien tai kirurgian poliklinikalla)?**

☐ En kertaakaan ☐ Kerran ☐ 2 kertaa ☐ 3 kertaa ☐ 4-6 kertaa ☐ yli 6 kertaa

**12. Kuinka monta kertaa viimeisen vuoden aikana olette käynyt vatsavaivojenne takia sairaalan päivystyspoliklinikalla (ensiapupoliklinikalla)?**

☐ En kertaakaan ☐ Kerran ☐ 2 kertaa ☐ 3 kertaa ☐ 4-6 kertaa ☐ yli 6 kertaa

**13. Kuinka monta kertaa viimeisen vuoden aikana olette käynyt vatsavaivojenne takia yksityislääkärin vastaanotolla? (Tässä ei tarkoiteta käyntejä yksityisellä lääkäriasemalla työterveyslääkärin luona)**

☐ En kertaakaan ☐ Kerran ☐ 2 kertaa ☐ 3 kertaa ☐ 4-6 kertaa ☐ yli 6 kertaa

**14. Kuinka usein viimeksi kuluneen 3 kuukauden aikana vatsaoireenne on haitannut Teidän työntekoanne töissä ollessanne?**

☐ Ei ollenkaan
☐ Harvemmin kuin 2 päivänä kuukaudessa
☐ 2-3 päivänä kuukaudessa
☐ 1-2 päivänä viikossa
☐ 3 päivänä viikossa tai useammin
☐ En ole ollut töissä viimeisten 3 kuukauden aikana

**15. Kuinka usein viimeksi kuluneen 3 kuukauden aikana olette käyttänyt vatsavaivojenne takia jotain seuraavista reseptivapaista "närästyslääkkeistä": Balancid, Gaviscon, Link, Magnesiamaito, Novaluzid, PeeHoo, PH maxi, Rennie, Alsucral, Antepsin?**

☐ En kertaakaan
☐ Harvemmin kuin 2 kertaa kuukaudessa
☐ Keskimäärin 2-3 kertaa kuukaudessa
☐ Keskimäärin 1-2 kertaa viikossa
☐ Keskimäärin 3-5 kertaa viikossa
☐ Päivittäin tai lähes päivittäin

**16. Kuinka usein viimeksi kuluneen 3 kuukauden aikana olette käyttänyt vatsavaivojenne takia jotain seuraavista mahan suolahapon eritystä vähentävistä lääkkeistä: Esofex, Ranicur, Ranil, Ranimex, Ranitidine, Ranitidin, Ranixal, Zantac, Pepcid, Pepcidin, Nizax?**

☐ En kertaakaan
☐ Harvemmin kuin 2 kertaa kuukaudessa
☐ Keskimäärin 2-3 kertaa kuukaudessa
☐ Keskimäärin 1-2 kertaa viikossa
☐ Keskimäärin 3-5 kertaa viikossa
☐ Päivittäin tai lähes päivittäin

**17. Kuinka usein viimeksi kuluneen 3 kuukauden aikana olette käyttänyt vatsavaivojenne takia jotain seuraavista mahan suolahapon eritystä vähentävistä lääkkeistä: Lanzo, Losec, Nexium, Pariet, Somac?**

☐ En kertaakaan
☐ Harvemmin kuin 2 kertaa kuukaudessa
☐ Keskimäärin 2-3 kertaa kuukaudessa
☐ Keskimäärin 1-2 kertaa viikossa
☐ Keskimäärin 3-5 kertaa viikossa
☐ Päivittäin tai lähes päivittäin

**18. Kuinka usein viimeksi kuluneen 3 kuukauden aikana olette käyttänyt vatsavaivojenne takia reseptivapaata kipulääkettä, kuten Aspirin, Disperin, Primaspan, Burana, Ibusal, Ketomex, Ketorin, Orudis, Panadol, Para-tabs?**

☐ En kertaakaan
☐ Harvemmin kuin 2 kertaa kuukaudessa
☐ Keskimäärin 2-3 kertaa kuukaudessa
☐ Keskimäärin 1-2 kertaa viikossa
☐ Keskimäärin 3-5 kertaa viikossa
☐ Päivittäin tai lähes päivittäin

**19. Kuinka usein viimeksi kuluneen 3 kuukauden aikana olette käyttänyt vatsavaivojenne takia jotain seuraavista ripulilääkkeistä: Imocur, Imodium, Lopex, Carbo medicinalis, Tannopon?**

☐ En kertaakaan
☐ Harvemmin kuin 2 kertaa kuukaudessa
☐ Keskimäärin 2-3 kertaa kuukaudessa
☐ Keskimäärin 1-2 kertaa viikossa
☐ Keskimäärin 3-5 kertaa viikossa
☐ Päivittäin tai lähes päivittäin

**20. Kuinka usein viimeksi kuluneen 3 kuukauden aikana olette käyttänyt vatsavaivojenne takia jotain seuraavista ummetuksen hoitoon tarkoitetuista lääkkeistä: Pursennid, Sennapur, Metalax, Toilax, Laxoberon, Duphalac, Levolac, Loraga, Movicol, Klyx, Microlax?**

☐ En kertaakaan
☐ Harvemmin kuin 2 kertaa kuukaudessa
☐ Keskimäärin 2-3 kertaa kuukaudessa
☐ Keskimäärin 1-2 kertaa viikossa
☐ Keskimäärin 3-5 kertaa viikossa
☐ Päivittäin tai lähes päivittäin

**21. Kuinka usein viimeksi kuluneen 3 kuukauden aikana olette käyttänyt vatsavaivojenne takia jotain seuraavista kuituvalmisteista: Agiocur, Agiolax, Laxamucil, Vi-Siblin?**

☐ En kertaakaan
☐ Harvemmin kuin 2 kertaa kuukaudessa
☐ Keskimäärin 2-3 kertaa kuukaudessa
☐ Keskimäärin 1-2 kertaa viikossa
☐ Keskimäärin 3-5 kertaa viikossa
☐ Päivittäin tai lähes päivittäin

**22. Kuinka usein viimeksi kuluneen 3 kuukauden aikana olette käyttänyt vatsavaivojenne takia jotain seuraavista suolistoperäisiä kiputiloja lievittävistä reseptilääkkeistä: Buscopan, Egazil Duretter, Gastrodyn comp, Librax, Spasmo-Oxepam, Litalgin?**

☐ En kertaakaan
☐ Harvemmin kuin 2 kertaa kuukaudessa
☐ Keskimäärin 2-3 kertaa kuukaudessa
☐ Keskimäärin 1-2 kertaa viikossa
☐ Keskimäärin 3-5 kertaa viikossa
☐ Päivittäin tai lähes päivittäin

**23. Kuinka usein viimeksi kuluneen 3 kuukauden aikana olette käyttänyt vatsavaivojenne takia jotain seuraavista suoliston toimintaan vaikuttavista reseptilääkkeistä: Metopram, Primperan, Prepulsid, Doryl, Mestinon, Ubretid?**

☐ En kertaakaan
☐ Harvemmin kuin 2 kertaa kuukaudessa
☐ Keskimäärin 2-3 kertaa kuukaudessa
☐ Keskimäärin 1-2 kertaa viikossa
☐ Keskimäärin 3-5 kertaa viikossa
☐ Päivittäin tai lähes päivittäin

**24. Onko Teillä ollut viimeksi kuluneen 3 kuukauden aikana ollut käytössä jokin seuraavista masennus- eli depressiolääkkeistä:**

**a) Triptyl, Klotriptyl, Saroten, Pertriptyl, Suprium, Doxal, Tolvon?**
☐ Kyllä ☐ Ei

**b) Seronil, Seromex, Fontex, Fevarin, Seroxat, Cipramil?**
☐ Kyllä ☐ Ei

**c) Jokin muu masennuslääke? Mikä?** (Kirjoittakaa lääkkeen kauppanimi viivalle)

_____

_____

**25. Oletteko käyttänyt viimeksi kuluneen 3 kuukauden aikana vatsavaivojenne hoitoon joitakin muita kuin edellisissä kysymyksissä mainittuja lääkkeitä?**

☐ En ☐ Kyllä, mitä lääkkeitä? (Kirjoittakaa lääkkeiden kauppanimet viivalle)

_____

_____

**26. Minkä ikäinen olitte, kun vatsavaivanne alkoivat?**

☐ Alle 20 vuotta ☐ 20-29 vuotta ☐ 30-39 vuotta ☐ 40-44 vuotta
☐ 45-49 vuotta ☐ 50-54 vuotta ☐ 55-59 vuotta ☐ 60-65 vuotta

**27. Onko lähisuvussanne (vanhemmillanne, sisaruksillanne tai lapsillanne) seuraavia sairauksia:**

| | | | |
|---|---|---|---|
| Paksu- tai peräsuolen syöpä? | ☐ Ei | ☐ Kyllä | ☐ En tiedä |
| Haavainen paksusuolitulehdus? | ☐ Ei | ☐ Kyllä | ☐ En tiedä |
| Crohnin tauti? | ☐ Ei | ☐ Kyllä | ☐ En tiedä |
| Keliakia? | ☐ Ei | ☐ Kyllä | ☐ En tiedä |

**28. Onko Teillä esiintynyt viimeksi kuluneen vuoden aikana vatsavaivojenne yhteydessä seuraavia oireita:**

| | | |
|---|---|---|
| Verta ulosteissa? | ☐ Ei | ☐ Kyllä |
| Yli 3 kg laihtuminen ilman laihdutustarkoitusta? | ☐ Ei | ☐ Kyllä |
| Kuumeilua? | ☐ Ei | ☐ Kyllä |
| Herääminen yöllä vatsaoireiden takia? | ☐ Ei | ☐ Kyllä |
| Oireiden jatkuva paheneminen ilman lievempioireisia välikausia? | ☐ Ei | ☐ Kyllä |

**Seuraavat kysymykset liittyvät yleiseen terveydentilaanne. Rastittakaa <u>yksi vaihtoehto, joka parhaiten kuvaa tilannettanne.</u>**

**29. Onko terveytenne yleisesti ottaen…**

☐ erinomainen
☐ varsin hyvä
☐ hyvä
☐ tyydyttävä
☐ huono

**30. Jos vertaatte nykyistä terveydentilaanne vuoden takaiseen, onko terveytenne yleisesti ottaen…**

☐ tällä hetkellä paljon parempi kuin vuosi sitten
☐ tällä hetkellä jonkin verran parempi kuin vuosi sitten
☐ suunnilleen samanlainen
☐ tällä hetkellä jonkin verran huonompi kuin vuosi sitten
☐ tällä hetkellä paljon huonompi kuin vuosi sitten

**Seuraavassa luetellaan erilaisia päivittäisiä toimintoja. Rajoittaako terveydentilanne nykyisin suoriutumistanne seuraavista päivittäisistä toiminnoista? Jos rajoittaa, kuinka paljon?** (Merkitkää joka riville yksi rasti sopivaan ruutuun)

| | Kyllä, rajoittaa paljon | Kyllä, rajoittaa hiukan | Ei rajoita lainkaan |
|---|---|---|---|
| **31.** Huomattavia ponnistuksia vaativat toiminnat (esimerkiksi juokseminen, raskaiden tavaroiden nostelu, rasittava urheilu) | ☐ | ☐ | ☐ |
| **32.** Kohtuullisia ponnistuksia vaativat toiminnat, kuten pöydän siirtäminen, imurointi, keilailu | ☐ | ☐ | ☐ |
| **33.** Ruokakassien nostaminen tai kantaminen | ☐ | ☐ | ☐ |
| **34.** Nouseminen portaita useita kerroksia | ☐ | ☐ | ☐ |
| **35.** Nouseminen portaita yhden kerroksen | ☐ | ☐ | ☐ |
| **36.** Vartalon taivuttaminen, polvistuminen, kumartuminen | ☐ | ☐ | ☐ |
| **37.** Noin kahden kilometrin matkan kävely | ☐ | ☐ | ☐ |
| **38.** Noin puolen kilometrin matkan kävely | ☐ | ☐ | ☐ |
| **39.** Noin 100 metrin matkan kävely | ☐ | ☐ | ☐ |
| **40.** Kylpeminen tai pukeutuminen | ☐ | ☐ | ☐ |

**Onko Teillä viimeisen 4 viikon aikana ollut RUUMIILLISEN TERVEYDENTILANNE TAKIA alla mainittuja ongelmia työssänne tai muissa tavanomaisissa päivittäisissä tehtävissänne?** (Rastittakaa yksi ruutu joka riviltä)

| | Kyllä | Ei |
|---|---|---|
| **41.** Vähensitte työhön tai muihin tehtäviin käyttämäänne aikaa | ☐ | ☐ |
| **42.** Saitte aikaiseksi vähemmän kuin halusitte | ☐ | ☐ |
| **43.** Terveydentilanne asetti Teille rajoituksia joissakin työ- tai muissa tehtävissä | ☐ | ☐ |
| **44.** Töistänne tai tehtävistänne suoriutuminen tuotti vaikeuksia (olette joutunut esim. ponnistelemaan tavallista enemmän) | ☐ | ☐ |

**Onko Teillä viimeisen 4 viikon aikana ollut TUNNE-ELÄMÄÄN LIITTYVIEN VAIKEUKSIEN (esim. masentuneisuus tai ahdistuneisuus) takia alla mainittuja ongelmia työssänne tai muissa tavanomaisissa päivittäisissä tehtävissänne?** (Rastittakaa yksi ruutu joka riviltä)

| | Kyllä | Ei |
|---|---|---|
| **45.** Vähensitte työhön tai muihin tehtäviin käyttämäänne aikaa | ☐ | ☐ |
| **46.** Saitte aikaiseksi vähemmän kuin halusitte | ☐ | ☐ |
| **47.** Ette suorittanut töitänne tai muita tehtäviänne yhtä huolellisesti kuin tavallisesti | ☐ | ☐ |

**48. MISSÄ MÄÄRIN ruumiillinen terveydentilanne tai tunne-elämän vaikeudet ovat viimeisen 4 viikon aikana häirinneet tavanomaista (sosiaalista) toimintaanne perheen, ystävien, naapureiden tai muiden ihmisten parissa?** (Rastittakaa yksi vaihtoehto)

☐ Ei lainkaan
☐ Hieman
☐ Kohtalaisesti
☐ Melko paljon
☐ Erittäin paljon

**49. Kuinka voimakkaita ruumiillisia kipuja Teillä on ollut viimeisen 4 viikon aikana?** (Rastittakaa yksi vaihtoehto)

☐ Ei lainkaan
☐ Hyvin lieviä
☐ Lieviä
☐ Kohtalaisia
☐ Voimakkaita
☐ Erittäin voimakkaita

**50. Kuinka paljon kipu on häirinnyt tavanomaista työtänne (kotona tai kodin ulkopuolella) viimeisen 4 viikon aikana?** (Rastittakaa yksi vaihtoehto)

☐ Ei lainkaan
☐ Hieman
☐ Kohtalaisesti
☐ Melko paljon
☐ Erittäin paljon

**Seuraavat kysymykset koskevat sitä, miltä Teistä on tuntunut viimeisen 4 viikon aikana. Merkitkää kullekin riville yksi rasti siihen kohtaan, joka parhaiten kuvaa tuntemuksianne.**

| | koko ajan | suurimman osan aikaa | huomattavan osan aikaa | jonkin aikaa | vähän aikaa | en lainkaan |
|---|---|---|---|---|---|---|
| **51.** Tuntenut olevanne täynnä elinvoimaa | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ |
| **52.** Ollut hyvin hermostunut | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ |
| **53.** Tuntenut mielialanne niin matalaksi, ettei mikään ole voinut Teitä piristää | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ |
| **54.** Tuntenut itsenne tyyneksi ja rauhalliseksi | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ |
| **55.** Ollut täynnä tarmoa | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ |
| **56.** Tuntenut itsenne alakuloiseksi ja apeaksi | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ |
| **57.** Tuntenut itsenne "loppuunkuluneeksi" | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ |
| **58.** Ollut onnellinen | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ |
| **59.** Tuntenut itsenne väsyneeksi | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ |

**60. KUINKA SUUREN OSAN AJASTA ruumiillinen terveydentilanne tai tunne-elämän vaikeudet ovat viimeisen 4 viikon aikana häirinneet tavanomaista sosiaalista toimintaanne (ystävien, sukulaisten, muiden ihmisten tapaaminen)?** (rastittakaa yksi vaihtoehto)

☐ Koko ajan
☐ Suurimman osan aikaa
☐ Jonkin aikaa
☐ Vähän aikaa
☐ Ei lainkaan

**Kuinka hyvin seuraavat väittämät pitävät paikkansa Teidän kohdallanne?** (merkitkää yksi rasti joka riville)

| | pitää ehdottomasti paikkansa | pitää enimmäkseen paikkansa | en osaa sanoa | enimmäkseen ei pidä paikkaansa | ehdottomasti ei pidä paikkaansa |
|---|---|---|---|---|---|
| **61.** Minusta tuntuu, että sairastun jonkin verran helpommin kuin muut ihmiset | ☐ | ☐ | ☐ | ☐ | ☐ |
| **62.** Olen vähintään yhtä terve kuin kaikki muutkin tuntemani ihmiset | ☐ | ☐ | ☐ | ☐ | ☐ |
| **63.** Uskon, että terveyteni tulee heikkenemään | ☐ | ☐ | ☐ | ☐ | ☐ |
| **64.** Terveyteni on erinomainen | ☐ | ☐ | ☐ | ☐ | ☐ |

**Tarkistakaa vielä, että olette vastannut kaikkiin kysymyksiin ja palauttakaa kaavake oheisessa palautuskuoressa, jonka postimaksu on jo maksettu puolestanne.**

**KIITOS YHTEISTYÖSTÄNNE!**